A CLINICAL STUDY OF 150 CASES OF

HERPES ZOSTER

Dissertation submitted to

THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY

CHENNAI-600032

APRIL2017

In partial fulfillment of the requirements for the award of

M.D.DEGREE IN

DERMATOLOGY, VENEREOLOGY AND LEPROLOGY (BRANCHXII)

COIMBATORE MEDICAL COLLEGE HOSPITAL,

COIMBATORE. DEPARTMENT OF DERMATOLOGY,

VENEREOLOGY AND LEPROLOGY

DECLARATION

I **Dr. VITHYA. R** solemnly declare that the dissertation entitled **"A clinical study of 150 cases of herpes zoster"** is a bonafide work done by me at Coimbatore Medical College Hospital during the year July 2015 to June 2016 under the guidance & supervision of **Dr.P.P.Ramasamy M.D., D.D.**, Professor & Head of Department, Department of Dermatology, Coimbatore Medical College & Hospital.

The dissertation is submitted to Dr.MGR Medical University towards partial fulfillment of requirement for the award of MD degree branch XII Dermatology, Venereology and Leprology.

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Date :

GUIDE
Dr.P.P.Ramasamy M.D.,D.D.,
Professor & HOD, Department of Dermatology,
Coimbatore Medical College & Hospital.

Date :

Dr.P.P.Ramasamy M.D.,D.D.,
Professor & HOD, Department of Dermatology,
Coimbatore Medical College & Hospital.

Date :

Dr.A.Edwin Joe M.D.,B.L.,
Dean,
Coimbatore Medical College & Hospital,
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Coimbatore Medical College

COIMBATORE, TAMILNADU, INDIA - 641 014

(Affiliated to The Tamilnadu Dr. MGR Medical University, Chennai)

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CERTIFICATE

Name of the Candidate : DR.VITHYA.R

Course : M.D. DERMATOLOGY

Period of Study : 2014 - 2017

College : COIMBATORE MEDICAL COLLEGE

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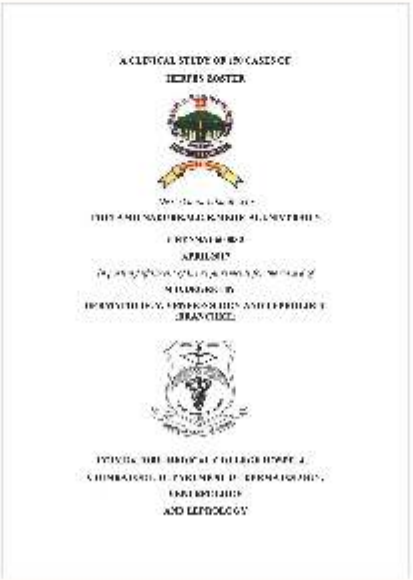

A CLINICAL STUDY OF 150 CASES OF
HERPES ZOSTER

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AND DERMATOLOGY

ABSTRACT

Title

A clinical study of 150 cases of herpes zoster

Background and objectives

Herpes zoster is caused by the reactivation of latent varicella zoster virus. The incidence of zoster increases with age. It is characterized by prodromal pain and grouped vesicles in unilateral dermatome. Post herpetic neuralgia is the most intractable and debilitating complication in older age group.

A clinical study was done to find the evolution, distribution and the complications of herpes zoster.

Methodology:

A total of 150 cases of herpes zoster attending outpatient department of dermatology and venereology, Coimbatore medical college hospital were included in the study after obtaining the consent. Detailed history, thorough physical examinations and relevant investigations were done.

Results:

The highest age incidence of the disease was seen in the 6^{th} decade of life. There was a male predominance with sex ratio of 1.5:1

Almost about two third of patients had prodromal symptoms with pain as common symptom. Thoracic segment was the commonly involved dermatome. Ninety two percent of the patients gave strong history of chicken pox in the past. Post herpetic neuralgia was the commonest complication (22 %) and the incidence of PHN increased with increasing age. The other complications seen were secondary bacterial infection and scarring.

ABBREVIATIONS

VZV	Varicella Zoster Virus
PHN	Post Herpetic Neuralgia
HIV	Human Immune Deficiency virus
ACV	Acyclovir
TB	Tuberculosis
CDC	Centers for Disease Control and Prevention
FDA	Food and Drug Administration
OPD	Out Patient Department
CBC	Complete Blood Count
RBS	Random Blood Sugar
H/O	History of
MNG	Multi Nucleated Giant

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INTRODUCTION

Varicella zoster virus is the causative organism of varicella and herpes zoster infection[1]. VZV is transmitted by droplet infection and also direct contact with chickenpox or herpes zoster patients[2].

Varicella is the result of primary VZV infection characterised by viremia and wide spread cutaneous eruption, commonly occurring in younger age group. The virus persists in the latent form in the sensory ganglion following primary infection.

Herpes zoster is caused by the reactivation of latent virus, more common in adult. On reactivation, virus replicates, travels down in the sensory nerve and infect the skin. It is characterised by unilateral, dermatomal pain and vesicle. Most significant clinical manifestation of zoster is prodromal pain and post herpetic neuralgia.

The risk factors for reactivation of VZV are old age, stress, diabetes, immunocompromised states like HIV infection, leukaemia, lymphoma and usage of cancer chemotherapy medications and radiotherapy[3].

Zoster is diagnosed by clinical appearance of unilateral grouped vesicles arranged in dermatomal pattern with prodromal pain and confirmed by Tzanck smear, viral culture and serological investigation.

Antiviral therapy for zoster accelerates cutaneous healing and reduce the severity of zoster associated pain and other complications.

This study has been under taken to determine the incidence, evolution and distribution of herpes zoster and incidence of post herpetic neuralgia.

AIMS AND OBJECTIVES

1. To study the evolution and distribution of herpes zoster.

2. To study the incidence of post herpetic neuralgia in herpes zoster.

REVIEW OF LITERATURE

HISTORY

Heberden distinguished chickenpox from small pox in 1767.Chicken pox is a French word meaning "CHICHE POIS" or "CHICK PEA" [4]

The origin of the word herpes is derived from the Greek word meaning "to creep". "Zoster" is derived from the Greek and Latin words meaning "gridle" or "belt" [5]

In 1875 Steiner transmitted VZV to the volunteers by inoculating the vesicular fluid of a person suffering from chicken pox[6].

In 1888 Von Bokay observed the association between the varicella and zoster[7]. Kundratitz (1922) and Bruusgarrd (1932) were then able to show that the same agent was the cause of both disease[8].

The histopathologic description of Herpes zoster was made by Lipschutz (1921)[9].

In 1943 Garland suggested that herpes zoster was the consequence of the reactivation of latent VZV[10].

In 1958 – VZV was isolated. Weller and colleagues[11] established that there were neither biologic nor immunologic differences between the viral agents isolated from patients with two clinical diseases, which was confirmed with restriction endonuclease analysis.

Intranuclear inclusions and multinucleated giant cells were described by Tyzzer in histopathology. In 1947 Tzanck identified multinucleated giant cells from the smear taken from the base of the blister. Hope Simpson recognised the importance of immune system in controlling zoster[13].

VIROLOGY

VZV is a double stranded DNA virus which belongs to alpha group of herpesviridae family[14]. The size is 180-200nm and the DNA contains 125000 base pairs which encodes about 75 protein.

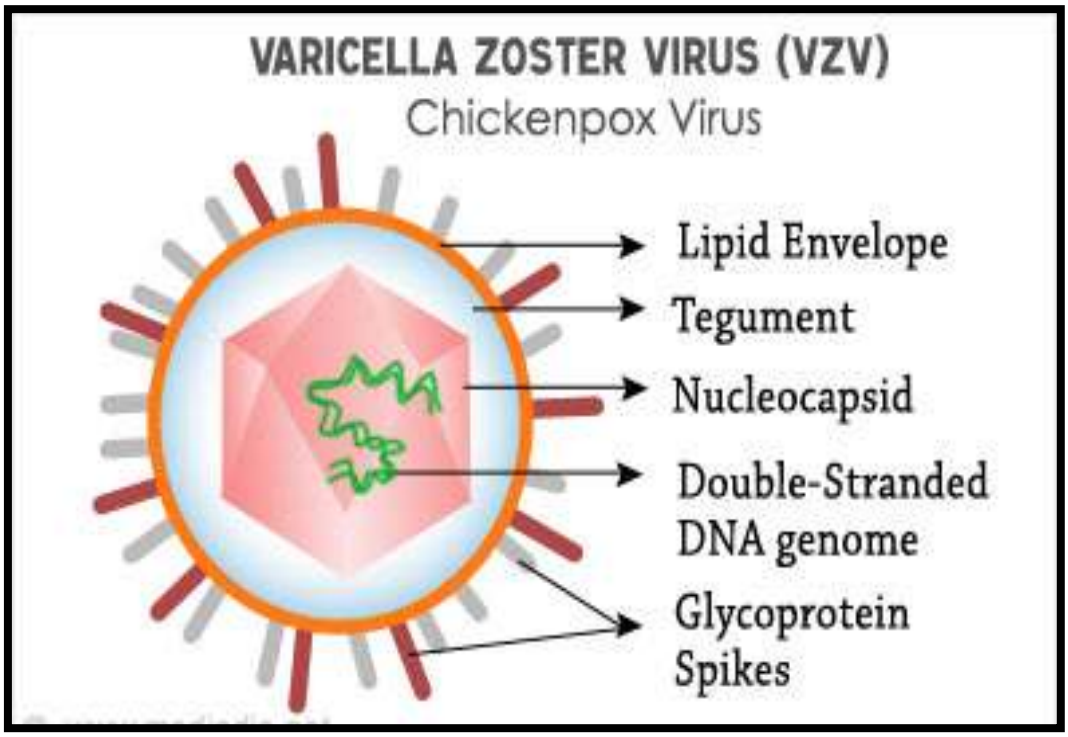


FIG: 1- STRUCTURE OF VARICELLA ZOSTER VIRUS

The nucleocapsid has a diameter of 90-95 nm, with icosapentahedral symmetry, and it protects the DNA core. It has 162 hexagonal capsomeres with central axial hollow[15].

The nucleocapsid is covered by an amorphous proteinaceous material called tegument. Tegument is surrounded by the envelope which is a lipid membrane and is derived from host cell membrane. It has five families of glycoprotein (gp1 –gp5)[16].

The enveloped viruses are infectious. The envelope is sensitive to detergent, ether and air drying. VZV is cell associated and it spreads from cell to cell by direct contact.

EPIDEMIOLOGY

The virus is more transmittable in temperate regions than in tropics. In temperate climate children are more prone whereas in tropics, it's the disease of adulthood.[15]

Herpes zoster primarily affects adult older than 50 years but may occur at any age. Person with a history of primary varicella have 20% life time chance of later developing HZ. The incidence and duration of zoster is rare in child hood, but it is more frequent in children who had primary varicella infection in the first year of life.[16]

The incidence of zoster in adult could increase if there is a decline in exposure of VZV in childhood as there is reduced immune boosting.

PATHOGENESIS [18, 19]

Varicella is one of the most contagious infections, 80-90% of susceptible contacts develop infection after the exposure. It is transmitted by respiratory droplets or by contact with infected lesions. The infectious period ranges from two days prior to five days after the onset of rash. There is no evidence that zoster can be acquired directly from contact with varicella and zoster.

VZV can be isolated from the vesicle and pustules in uncomplicated cases for up to seven days after the appearance of the rash and for much longer periods in immunocompromised individuals.

Following the entry of VZV through the mucosa of upper respiratory tract and oropharynx virus replicates within regional lymph nodes. Virus disseminate through the blood and lymphatics (primary viremia). It multiplies in the liver, spleen and other organs (secondary viremia) which seeds the entire body, 14 to 16 days post exposure. During this period virus invades capillary endothelial cells and travels to the epidermis. Virus subsequently spreads from mucocutaneous lesions to sensory nerve endings and sensory ganglion. It remains latent in dorsal root ganglion. On reactivation, replicates and produces painful ganglionitis. Virus spreads antidromically down the sensory nerve and produce intense neuritis. It is released from the sensory nerve endings in the skin, where it produces the characteristic cluster of zoster vesicles. It spreads from ganglionic infection proximally along the posterior nerve root to the meninges and cord result in local leptomeningitis and segmental myelitis. Rarely infection of the motor neurons in the anterior horn and inflammation of the anterior nerve root may cause local palsies. Extension of infection within the CNS results in meningoencephalitis and transverse myelitis. The following flow chart illustrates the pathogenesis of HZV.

Pathogenesis of VZV

Flow Chart - 1

Virus

↓

Conjunctiva/ mucosa of upper respiratory tract

↓

Regional lymphnode (first replications)

↓

Primary viremia (4 to-6 days after exposure)

↓

Second replications (liver, spleen)

↓

Secondary viremia (seeding the entire body)

↓

Virus invade capillary endothelial cells, capillaries and epidermis (14 -16 days after exposure)

↓

Sensory nerve ending

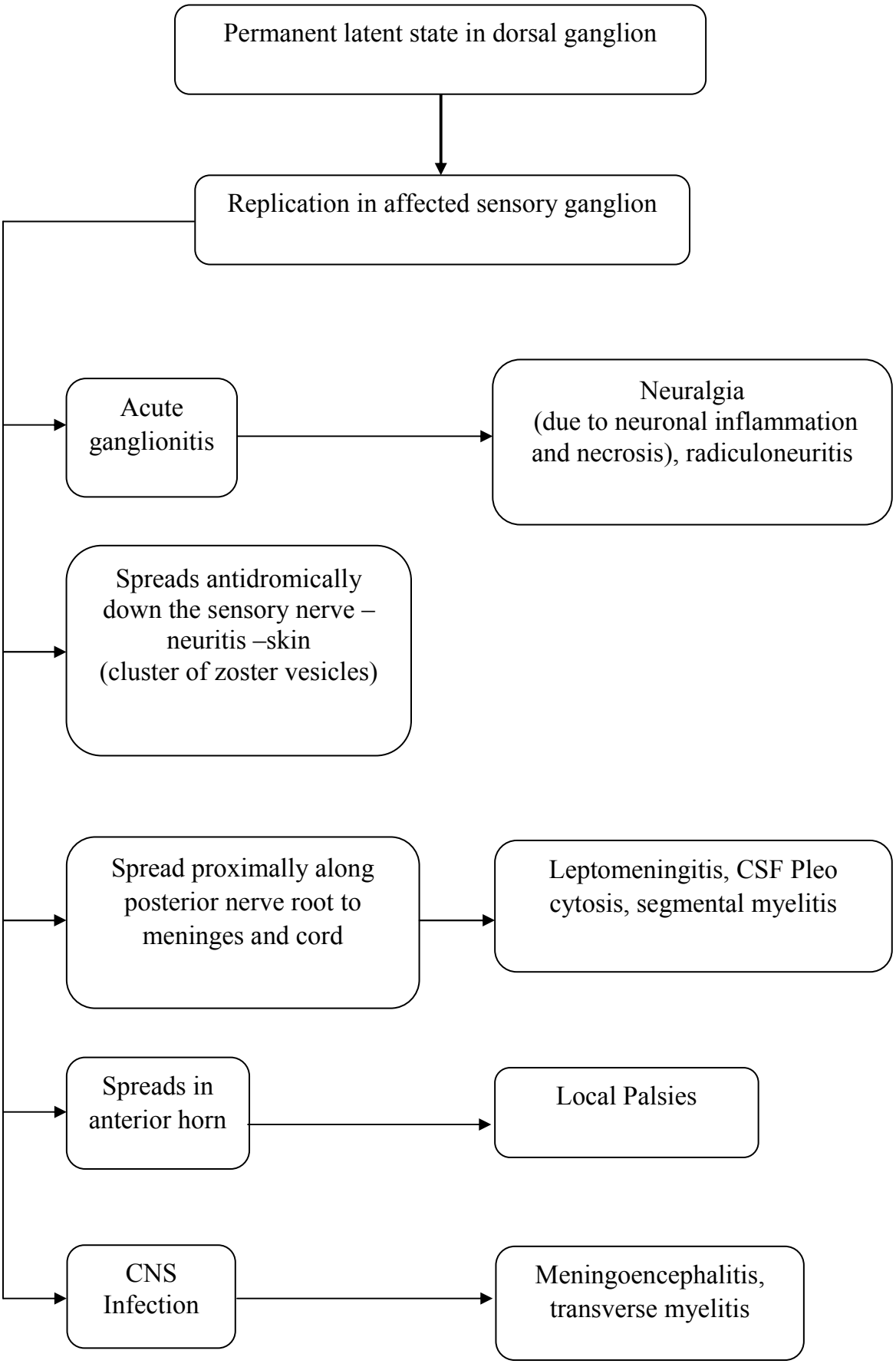
↓

Spreads centripetally along nerve fibres

↓

Permanent latent state in dorsal ganglion

Pathogenesis of Herpes zoster



PATHOGENESIS OF ZOSTER ASSOCIATED PAIN (ZAP) and POST- HERPETIC NEURALGIA

Pain is the major symptom of zoster. The term zoster associated pain refers to all pain accompanying, preceding, and following zoster. Post-herpetic neuralgia defined as persistence or recurrence of pain more than a month after the onset of zoster. Age is the most important factor for developing post herpetic neuralgia[20].

The quality of ZAP varies but three basic types have been described. The constant deep aching pain, the shooting- lancinating pain and triggered pain. Triggered pain is usually allodynia[21] or hyperalgasia.

Pathophysiology of pain:

Noxious stimuli activate free nerve endings in the skin to generate signals that are conveyed through unmyelinated Cfibres and small Aδ fibres to the neurons in the segmental dorsal root ganglion , then to the dorsal horn of the spinalcord. In the spinalcord they form synapses with second order neuron. Spinalcord neurons are subject to descending inhibitory signals from the brain. Inhibitory signals are mediated by the biogenic amines serotonin and norephinephrine. The net result of peripheral afferent input and decending inhibitory input is projected cephalalid, joining other ascending fibers in the contralateral

spinothalamic tract where it is integerated with input from brainstem and cortical areas for the perception of pain.[22]

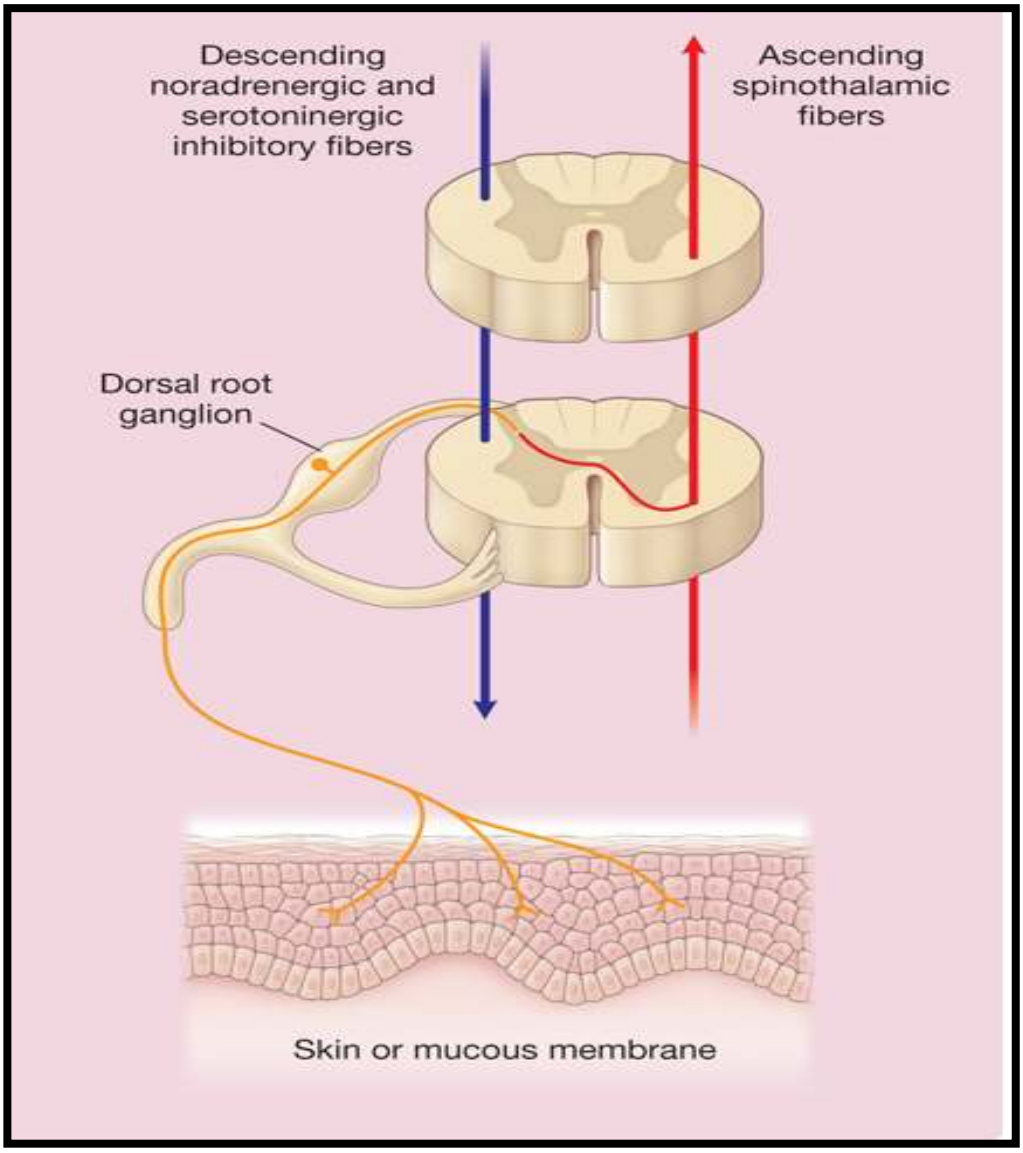


FIG: 2 NORMAL PAIN PATHWAY

Sensitization and de-afferentiation are two different mechanisms proposed to cause pain in zoster[21]. Nociceptors become sensitised, following injury resulting in ongoing discharge and hyper excitability. Prolonged impulses of the nociceptor enhances the dorsal horn neurons to afferent stimuli and expands the dorsal horn neurons receptive field leading to allodynia and hyperalgesia. In addition, neural destruction causes spontaneous activity in deafferented central neurons causing constant pain.

The anatomical and functional changes responsible for post herpetic neuralgia appear to be established in the early course of zoster. This would explain the correlation of initial pain severity and the presence of prodromal pain with the subsequent development of post herpetic neuralgia.[23]

HISTOPATHOLOGY

SKIN LESIONS

- **Initial stage:**

The earliest changes involve the epidermal cell nuclei which develop peripheral clumping of chromatin and a homogenous ground glass appearance, combined with ballooning of nucleus.

Vacuolization is the earliest cytoplasmic changes. These changes begin focally along the basal layer, but rapidly involve the entire epidermis.

- **Vesicular Stage:**

Intra epidermal vesicle results from the following types of degenerative changes. They are 1.Ballooning degeneration and 2. Reticular degeneration.

Ballooning degeneration is peculiar to viral vesicles. The affected cells swell and lose their attachment from the adjacent cells, thus separating from them (secondary acantholysis).[24] The cytoplasm of these cells becomes homogenous and intensively eosinophilic with multiple nucleous (Tzanck cells).[11] At times the basal layer of the epidermis is also destroyed and leading to the formation of a sub-epidermal vesicle. Ballooning degeneration is found mainly at the base of the vesicle.

Reticular degeneration[24] is characterized by progressive hydropic swelling of epidermal cells, which become large and clear. The cells has fine cytoplasmic strands remaining at the edge. These eventually rupture and contribute to the formation of a vesicle. Reticular degeneration is seen on its superficial aspect and margin.

Multinucleated giant cells containing up to 15 nuclei are formed by fusion of epithelial cells containing eosinophilic intranuclear inclusion bodies known as Lipschutz bodies.[25]

- **Late stage:**

Eosinophilic intra nuclear inclusion bodies are found, particularly in ballooned cells. Neutrophils are present within vesicles. Neutrophilic and lymphocytic infiltration is present in the underlying dermis. Marked inflammation and vasculitis[26] have been noted in some lesions. If the vasculitis is severe, necrotizing lesions will be present. Eccrine duct involvement is also noted. The chronic verrucous lesions shows hyperkeratosis, verruciform acanthosis and virus-induced cytopathic changes.[27]

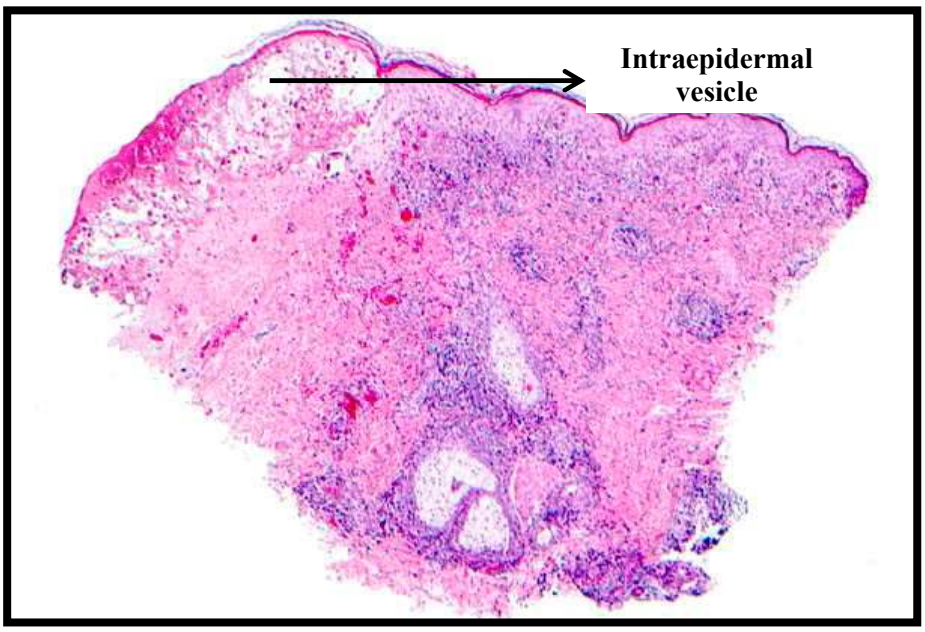


FIG: 3 HISTOPATHOLOGY OF HERPES ZOSTER

IMMUNOLOGY

Primary VZV infection induces both humoral and T cell mediated immunity. Cellular immunity is more important than humoral immunity for limiting the extent of primary varicella infection and for prevention of reactivation of latent virus. When cell mediated immunity decline, as occurs in aging or iatrogenic immunosuppression, reactivation of latent VZV occurs.[28]

During latency phase VZV has evolved several mechanisms to reduce the presentation of viral proteins to the immune system and thereby evade detection. It also evade the immune system by down regulating the expression of MHC class1 antigens on surface of infected cells.[19]

Clinical manifestations

Prodromal Stage:

The early manifestation of zoster is pain. The pain may be localised to same area or diffuse, deep boring or lancinating pain which may be constant or intermittent. The duration between the start of pain and the onset of the eruption averages 1.4 days in trigeminal zoster to 3.2 days in thoracic zoster.[29] The skin in the affected area becomes red followed by appearance of papules.

The pre eruptive pain may simulate myocardial infarction, pleurisy, duodenal ulcer, biliary colic, renal colic, appendicitis,

cholecystitis, prolapsed inter vertebral disc, early glaucoma, dental pain and headache.

In immunocompromised persons, pain is uncommon. Some patients have segmental neuralgia without cutaneous eruptions known as Zoster sine herpete or Zoster sine eruptione.[30]

Eruptive Stage:

The eruption begins as closely grouped erythematous papules and plaques which rapidly becomes vesicular and then pustular. Typically herpes zoster is unilateral, does not cross midline and is localised to a single dermatome of a single sensory ganglion (adjacent dermatomes are involved in 20%). Mucous membranes within the affected dermatomes are also involved. Localisation and unilateral distribution of skin rash in the area of dermatome is distinctive feature of zoster.

Vesicles form within 12-24 hours and evolve into pustules by the third day and crust in 7-10 days. New lesions continue to appear for 1–4 days, occasionally as long as 7 days. The draining lymph nodes of affected area may become enlarged and tender. Bilateral eruption and multidermatomal involvement is seen in HIV infected individuals.

The thoracic (53%), cervical (C.2, 3, 4, 20%), trigeminal (15%), and lumbosacral (11%) segments are commonly involved at all ages but the ophthalmic zoster increases with old age.

Resolution Stage:

As the eruption disappears, pain and the constitutional symptoms subside gradually. Uncomplicated cases in children and young adults, resolve completely within 2-3 weeks whereas it takes 3-4 weeks in elderly.[29]

TABLE: 1- CLINICAL MANIFESTATIONS OF HERPES ZOSTER

Time after Initial Symptoms	Cl inical Manifestations
	Reactivation of the virus may occur up to several decades after initial varicella infection
	↓
0 days	Prodrome of localized pain
	↓
3-7 days	Unilateral dermatomal rash with erythematous macules and papules
	↓
4-8	Vesicles
	↓
6-10	Pustules
	↓
10-14 days	Crusts
	↓
2 wk, up to 4-6	Complete Healing

REGIONAL DISTRIBUTION OF ZOSTER:

1. Trigeminal nerve zoster

Three branches of trigeminal nerve such as ophthalmic, maxillary and mandibular divisions are affected.

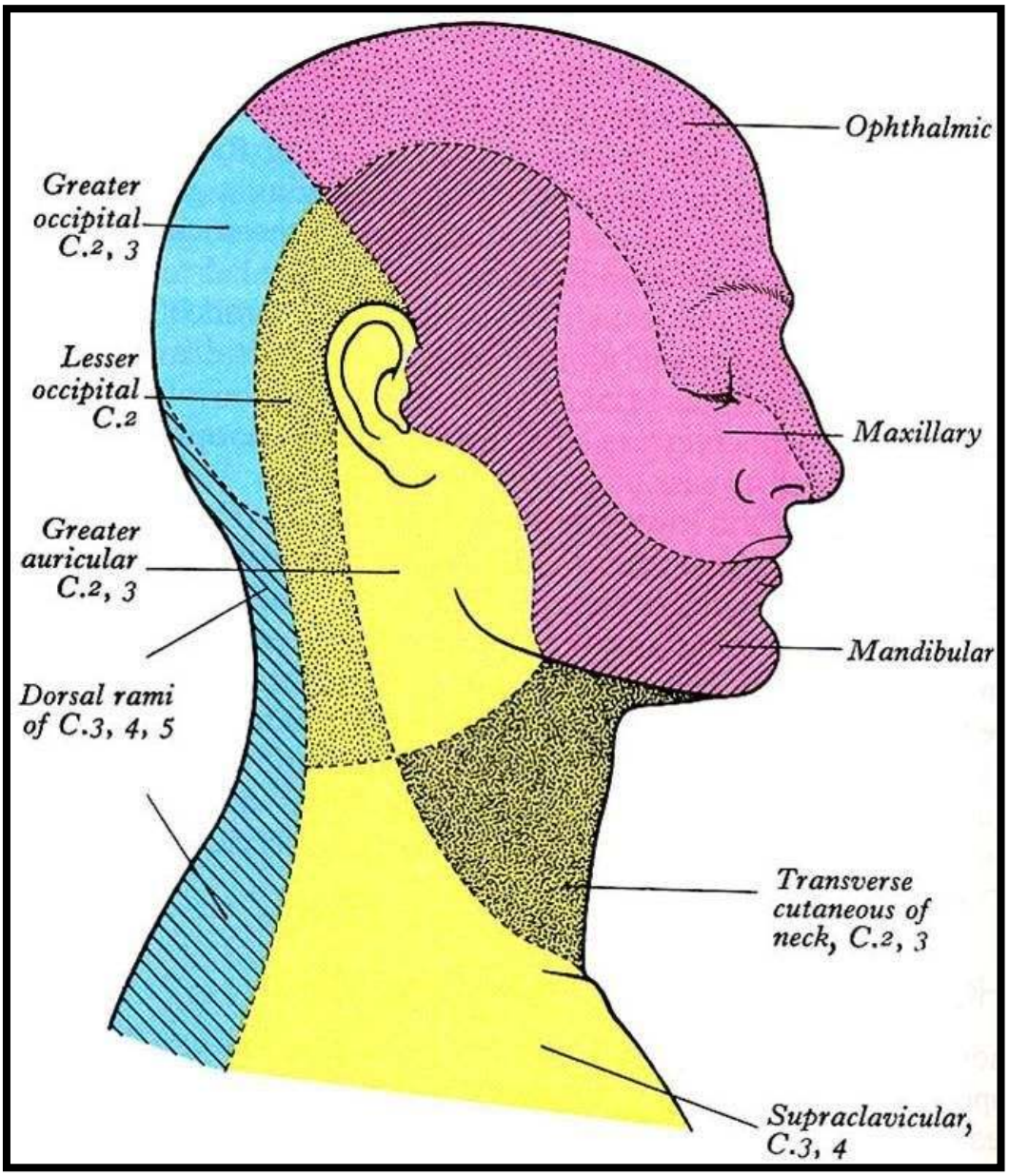


FIG: 4 DERMATOME OF FACE AND NECK

Ophthalmic zoster

Ophthalmic zoster accounts for about 10-15% of all zoster cases. Involvement of ophthalmic branch is five times more common than other branches of trigeminal nerve.[31, 32] The eye involvement is seen in about 20-70% of the cases.[33]

The vesicles extend from eye to vertex of the skull but terminates at the midline of forehead. Nasociliary nerve innervates eye as well as tip and side of the nose (Hutchinson's sign)[34] provides access of VZV to intraocular structures. Presence of Hutchinson's sign is associated with ocular complication such as uveitis, keratitis, conjunctivitis, conjunctival oedema, proptosis, scleritis, retinal vascular occlusion, ulceration and scarring of the eye lid. Involvement of ciliary ganglion produces Argyll Robertson pupil (accommodation reflex present, pupillary reflex absent), which may be temporary or permanent. Periocular involvement with sparing of eyeball occur in other sensory branches of trigeminal nerve. Ocular complications have the potential risk to produce visual impairment. Ophthalmic zoster occasionally associated with third and sixth cranial nerve palsies.

b. Maxillary zoster:

Vesicles appear on uvula, tonsillar area, and upper lip, mucosa of nose, pharynx and palate.[35]

c. Mandibular zoster:

Zoster of mandibular division produces vesicles on the anterior part of tongue, the floor of the mouth and the buccal mucosa. In mandibular zoster toothache may be the presenting symptom.[35]

2. Herpes zoster oticus:

Facial nerve supplies the external ear, the tonsillar fossa and adjacent soft palate by its vestigial sensory nerve fibres. Zoster in this sensory fibres produces pain and vesicles on the external auditory meatus, concha, pinna and tympanic membrane with unilateral loss of taste sensation on the anterior two third of tongue.

Swelling of the infected sensory fibres due to zoster leads to compression of adjacent neural structures in their course through the facial canal. Compression of motor fibres produces facial palsy.[36] Triad of facial palsy, ear pain and vesicles on ear constitutes Ramsey Hunt syndrome[37] or geniculate ganglion syndrome. Herpes zoster oticus constitutes 10% of facial palsy. Ramsey hunt syndrome have more severe paralysis at onset when compared with facial palsy (facial paralysis

without rash). Generally recovery from the motor paralysis is complete but residual weakness may be present.

Involvement of vestibulocochlear nerve is seen in some cases because of its close proximity to the geniculate ganglion within facial canal. It causes sensorineural hearing loss, dizziness, vertigo, tinnitus, and nystagmus.

3. Glossopharyngeal and vagal zoster:

Herpes pharyngitis and herpes laryngitis[38] occurs when jugular and petrosal ganglia are involved. Due to adjacent nature of the above two ganglia they are often involved in combination but may be affected separately. Vesicles appear on the palate, epiglottis, facial tonsils, and back of tongue. Glossopharyngeal zoster is also associated with ear pain, deep pharyngeal pain, laryngeal pain, palatal weakness, dysphagia and hyperesthesia.

4. Sacral zoster:

Sacral involvement (S2, S3or S4) of zoster causes urinary retention and urinary hesitation due to the migration of virus to the adjacent autonomic nerve. The symptoms are similar to those associated with passage of renal stones.

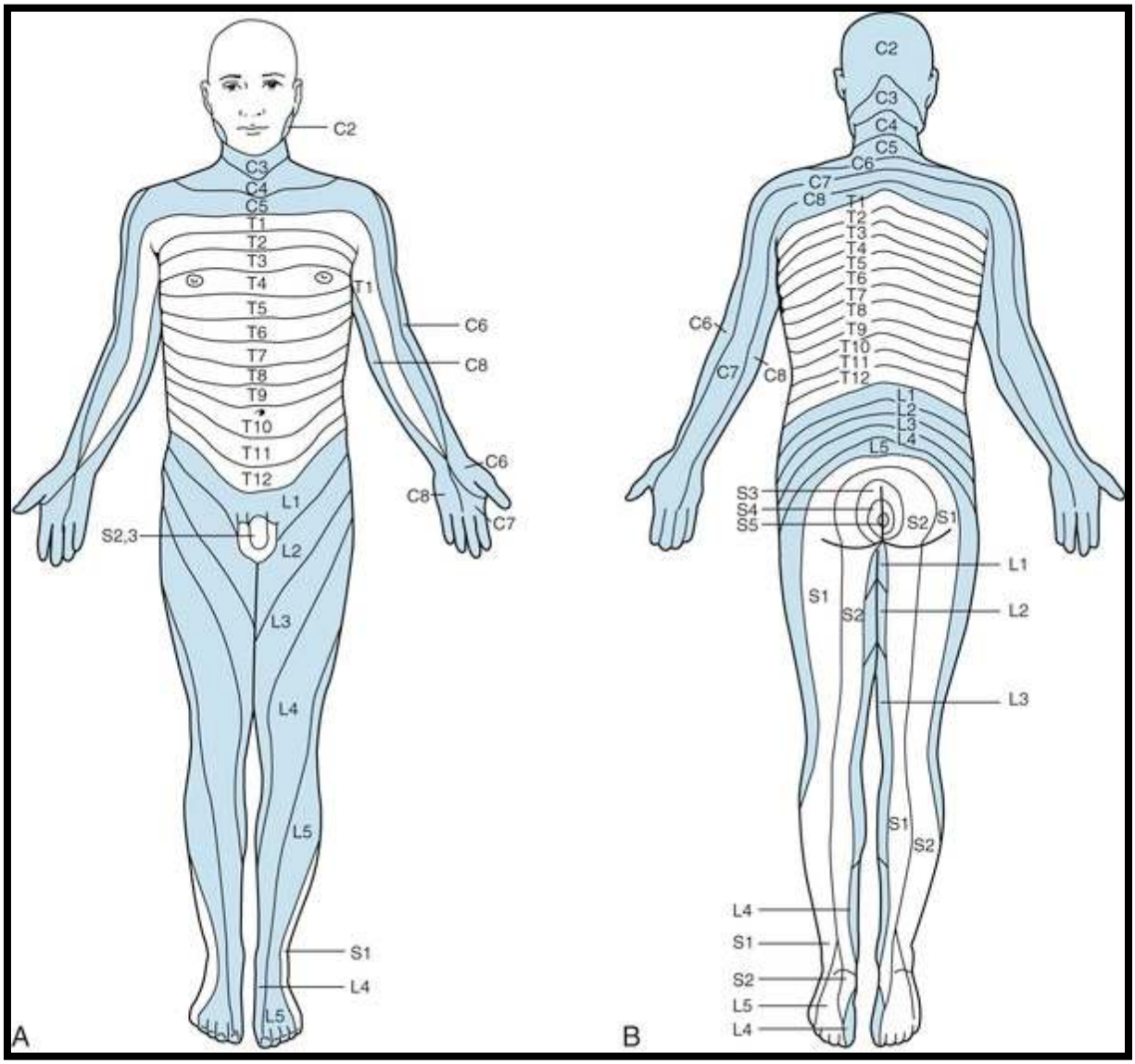


FIG:5 DERMATOMAL DISTRIBUTION

SPECIAL SITUATIONS

Zoster in HIV:

Herpes zoster has a high rate of dissemination (up to 40%) in HIV. Cutaneous dissemination is defined as more than twenty vesicles outside the area of primary and adjacent dermatome. This is followed by visceral dissemination into lungs, liver and brain. They have increased rate of neurological complications such as aseptic meningitis, radiculitis and myelitis.[39] Other manifestations are

a. Multidermatomal zoster
b. Chronic verrucous nodules[40]
c. Hyperkeratotic or erythematous cutaneous lesions resistant to acyclovir.

HIV infected patients suffer from multiple recurrences when their infection progresses. Zoster may recur in the same or different dermatomes or in several contiguous or non-contiguous dermatome.

Herpes zoster in pregnancy:

Irrespective of its occurrence in early or late pregnancy, herpes zoster does not cause deleterious effect on either mother or on the foetus or infant.[41] When compared to maternal varicella, zoster in early pregnancy is not associated with foetal damage.[42]

Herpes zoster in children:

Two percent of children those who are exposed to VZV in utero develops subclinical varicella and have increased risk for herpes zoster after birth. Immunocompromised children have multiple lesions with unusual dermatome and visceral involvement. Post herpetic neuralgia is uncommon in children.[43]

Herpes zoster after varicella immunization:

The occurrence of herpes zoster is less common after immunization than natural infection.

Complications of Herpes zoster

The sequale of herpes zoster include cutaneous, neurological, ophthalmic and visceral complications.

TABLE: 2 COMPLICATIONS OF HERPES ZOSTER

CUTANEOUS	NEUROLOGICAL	VISCERAL
Secondary infections	Post herpetic neuralgia	Gastritis
Scarring	Meningoencephalitis	Pneumonitis
Zoster gangrenosum	Transverse myelitis	Hepatitis
Cutaneous dissemination	Peripheral nerve palsies	Pericarditis
	Cranial nerve palsies	Cystitis
	Sensory loss	Esophagitis
	Hearing loss	
	Ocular complications	
	Granulomatous angitis	

1. Cutaneous complications:

The cutaneous complications are secondary bacterial infections, cutaneous necrosis, scarring, disseminated zoster and zoster gangrenosum.

2. Ocular complications:

The ocular complication have the potential to produce visual impairment. The complications are cicatricial lid retraction, optic neuritis, scleritis, uveitis, glaucoma,[44] panopthalmitis, corneal ulceration and keratitis.[45]

3. Neurological complications:

This includes meningoencephalitis, transverse myelitis, aseptic meningitis, motor and autonomic neuropathy, cranial nerve palsies and granulomatous angitis.

a. Meningoencephalitis:

Meningoencephalitis have been reported in 0.2-0.5% of herpes zoster patients.[46] Risk factors to develop meningoencephalitis are ophthalmic and disseminated zoster, immunosuppression and elderly patients. The symptoms mainly follows in the first two weeks after the skin lesions. The symptoms are fever, headache, vomiting, photophobia and altered mentation. The mortality rate is 10-20% and most survivors will recover completely.

b. Cranial nerve neuropathy:

Cranial nerve neuritis includes involvement of trigeminal nerve, facial and vestibule cochlear nerve,[47] vagus and glossopharyngeal nerve.[48]

c. Motor neuropathy:

Motor paresis occur in 5% of all cases of herpes zoster patients. More common in patient aged more than 60 years, cephalic zoster, and those with malignancy.[49] Motor neuropathy occurs during first 2-3 weeks after the onset of rash.

1. Herpes zoster of cervical and lumbar dermatome is associated with peripheral neuropathy of upper limb and lower limb respectively.
2. Dermatological dyspnoea occurs if C3-C5 roots are involved (diaphragmatic palsy)
3. Abdominal wall weakness and abdominal pseudo hernia occur in thoracic zoster.

Autonomic neuropathy:

Sacral zoster may produce urinary hesitancy, urinary retention colonic spasm, dilatation, obstipation, constipation, pseudo obstruction, and reduced anal sphincter tone.[50]

4. Visceral complications:

Patients with lymphoproliferative malignancy are associated with increased risk to develop visceral complications like pneumonitis, hepatitis, esophagitis, gastritis, pericarditis, and arthritis.[51]

Delayed complications of zoster

1. Post herpetic neuralgia (PHN)

2. Post herpetic itch

3. Granulomatous angitis:

This occurs as a delayed complications of CNS due to vasculopathies. Granulomatous angitis[52] is associated with trigeminal nerve zoster when its first branch gets affected. VZV gains access to CNS by direct extensions of trigeminal nerve along its intracranial branches and infect cerebral arteries. Patients present with headache and hemiplegia. It can be diagnosed by cerebral arteriography and CSF examination.

4. Isotopic phenomenon:

Defined as occurrence of an unrelated dermatological disease at the site of the previously healed lesion. Exact aetiology of this phenomenon is not known. Zoster induced local neuroimmune dysregulation of the dermal sensory nerve fibres has been suggested. Granulomatous conditions like granuloma annulare[53], scar sarcoid[54],

lichenoid and granulomatous dermatitis, granulomatous vasculitis appear over the healed zoster scars. Infiltratve lesions like pseudo lymphoma, xanthoma,and papulosquamous disorders like psoriasis, lichen planus, lichenoid GVHD may occur.

Diagnosis of Herpes zoster

Differential diagnosis for pre herpetic pain

1. Migraine
2. Myocardial infarction
3. Duodenal ulcer
4. Biliary colic
5. Renal colic
6. Acute appendicitis
7. Dental pain
8. Prolapsed intervertebral disc

Differential diagnosis of herpes zoster (Skin lesions):

Most likely

1. Zosteriform herpes simplex
2. Contact dermatitis
3. Insect bites
4. Poison ivy
5. Burns

Consider

1. Papular urticaria
2. Drug eruptions
3. Erythema multiforme
4. Scabies

Always rule out

1. Bullous pemphigoid
2. Dermatits herpitiformis
3. Pemphigus vulgaris

Clinical diagnosis:

History of prodromal pain and unilateral dermatomal distribution of skin lesion aid in clinical diagnosis in most of the patients. Some times zosteriform herpes simplex confused with zoster lesion. HSV is associated with recurrent lesions at the same site. Disseminated zoster from varicella is difficult to differentiate. Varicella has discrete erythematous vesicles whereas zoster has grouped vesicles.

Lab diagnosis:

Tzanck smears

Viral culture

Serological tests.

Tzanck smear:

Tzanck smear[11] is a bed side test to confirm the diagnosis. The material is scraped from base of an early vesicle, smeared on glass slide, and stained with Giemsa or hematoxylin and eosin or Papaniculaou stain. Presence of multinucleated giant cells and acidophilic intra nuclear inclusions confirm the diagnosis.

It cannot differentiate varicella and herpes zoster from herpes simplex virus. Sensitivity of the test is around 75%.

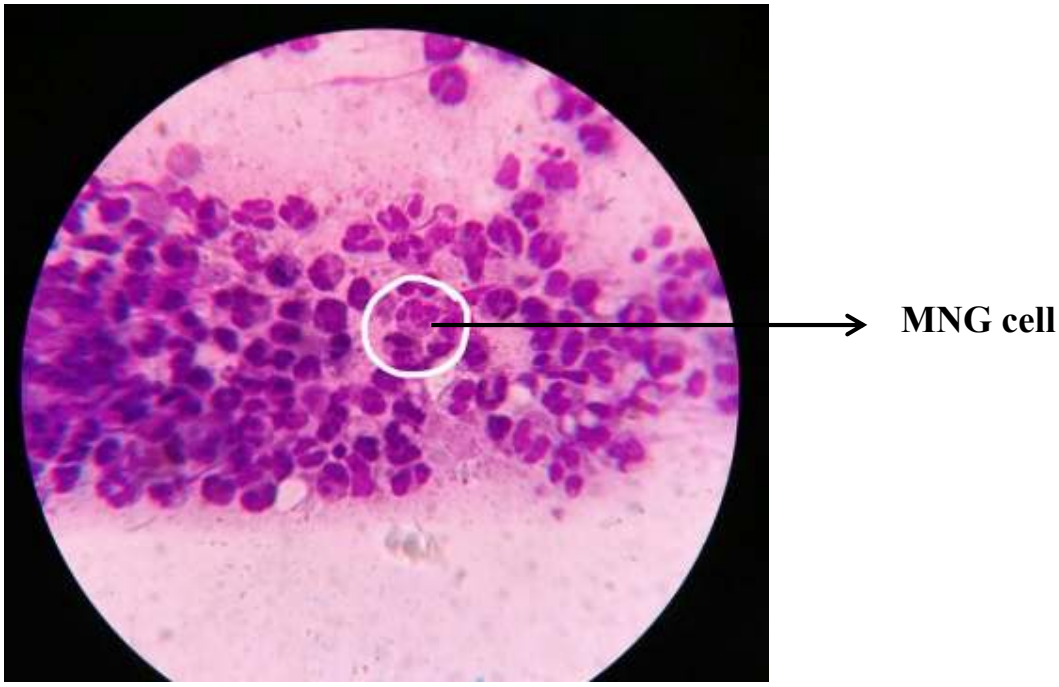


FIG: 6- Tzanck smear –multinucleated giant cells (MNG) seen

Histopathological examination:

The vesicles in varicella, herpes zoster, and herpes simplex are intra epidermal. Multinucleated keratinocytes, nuclear moulding and peripheral condensation[26,27] of the nucleoplasm are characteristic of infection with VZV and HSV. An underlying leukocytoclastic vasculitis is suggestive of VZV over HSV.

Viral culture:

Isolation of VZV by culture is the most specific test. Vesicle fluid, blood, cerebrospinal fluid, infected tissue are the material used as inoculum in human amnion, human fibroblast and Hela[55] or verocells. Cytopathic effects are produced after minimum of 48-72 hours.

Serological Tests:

The tests available to measure antibodies to VZV are

a. Enzyme linked immuno sorbent assay (ELISA)
b. Enzyme Immuno assay (EIA)
c. Radio Immuno assay (RIA)
d. Immune adherence haemagglutination assay (IAHA)
e. Complement fixation test (CFT)
f. Fluorescent antibody to membrane antigens (FAMA)
g. Latex agglutination test
h. Varicella zoster virus neutralization tests.

Recent Techniques:

1. **Polymerase Chain Reaction:**

   PCR is more useful for rapid and specific diagnosis of VZV infections. It aids in diagnosis of encephalomyelitis by examining CSF.[56]

2. **Nucleic acid probes**

MANAGEMENT:-

Includes general measures, reassurance, explaining the prognosis.

Treatment strategy is mainly to suppress the inflammation, pain, and infection. It includes topical and systemic therapy.

Topical therapy:

During the acute phase of zoster, the application of calamine lotion, cold compresses, corn starches or Burrows solution help to reduce local symptoms and hasten the drying of vesicular lesions.

Topical antiviral therapy is not recommended as it lacks efficacy in patients with zoster.[57]

Systemic therapy:

Antiviral drugs in herpes zoster

1. Prevent progression of eruption
2. Limit the extent, duration and severity of pain
3. Reduce the development of post herpetic neuralgia.

Initiation of antiviral drugs within 72 hours of onset of skin lesions is optimal, but it can be started up to seven days in persons aged more than 50 years and in immunocompromised individuals.

FDA approved antiviral drugs for herpes zoster are

1. Acyclovir
2. Valacyclovir
3. Famcyclovir

Acyclovir:

Acyclovir is an acrylic guanosine derivative, (9-2-hydroxyethoxymethyl guanine or acycloguanosine) most widely used antiviral drug.[58] Activation of ACV requires phosphorylation by herpes specific thymidine kinase before bi- and triphosphorylation by host cell enzyme. So it is selectively activated in virus infected cells.

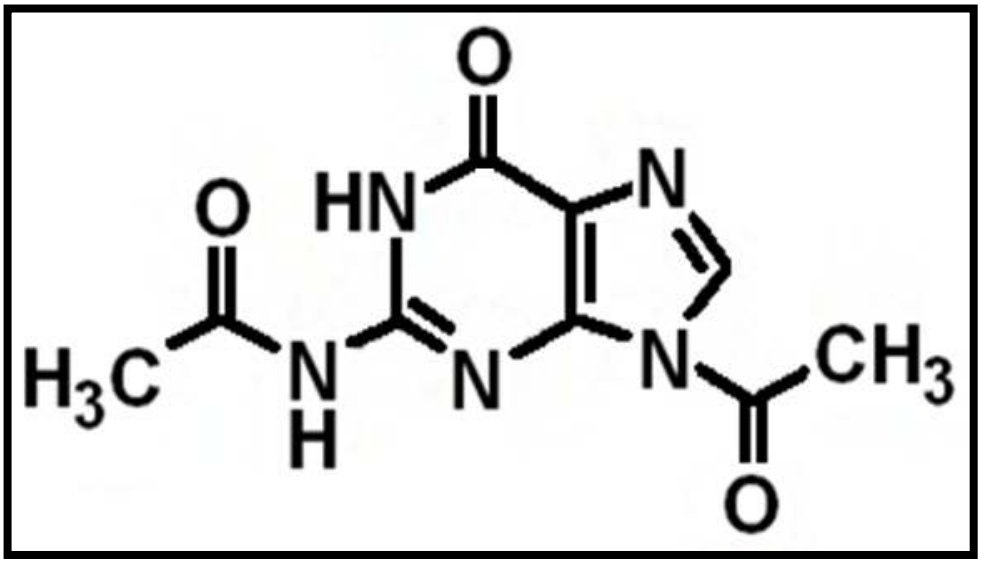


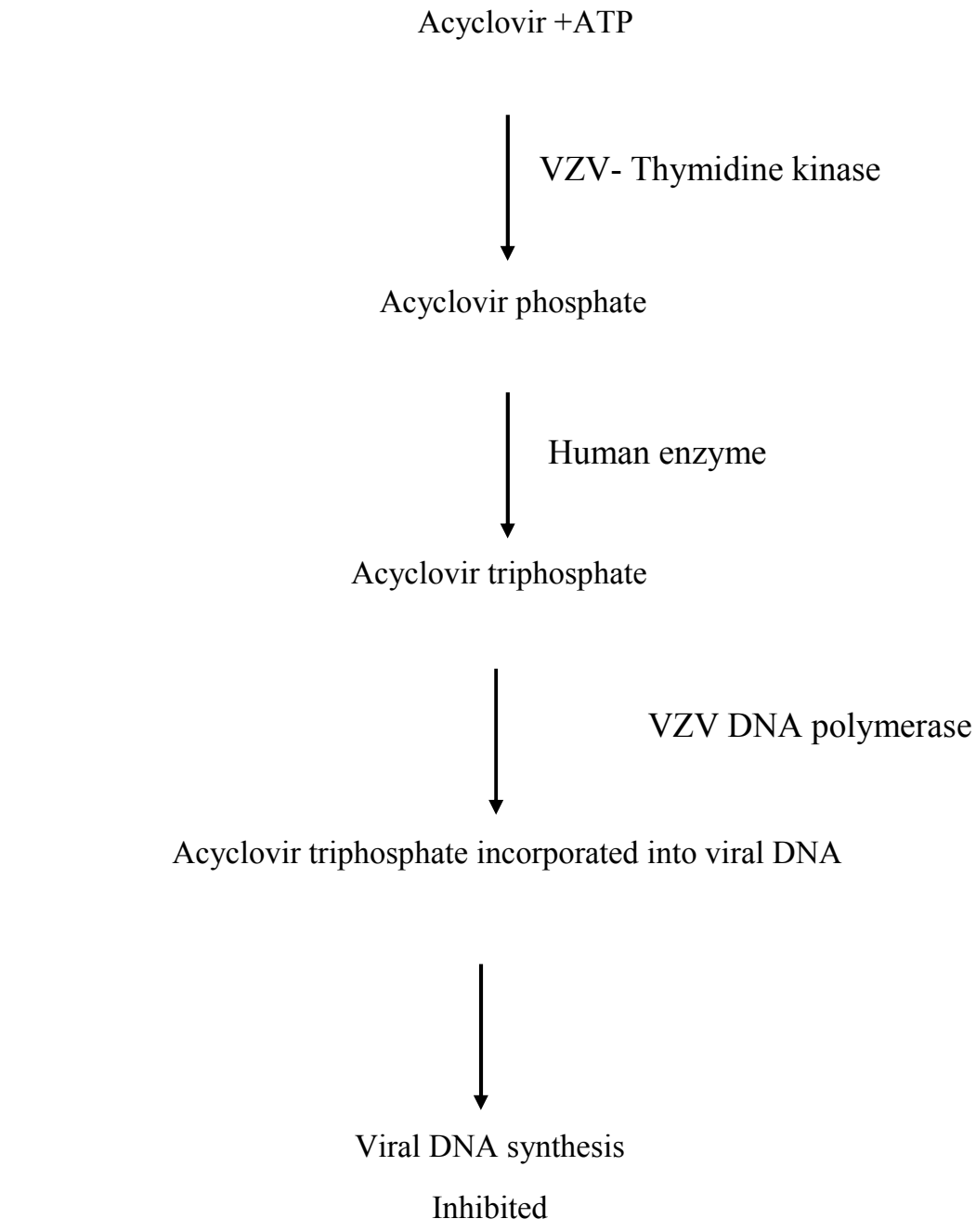
FIG: 7- STRUCTURE OF ACYCLOVIR

Acyclovir inhibits viral DNA synthesis by a competitive inhibition of deoxy GTP of viral DNA polymerase and by chain termination.

The following flow chart Illustrates mechanism of action of acyclovir.

MECHANISM OF ACTION OF ACYCLOVIR

FLOW CHART



Varicella zoster virus is less susceptible to acyclovir than herpes simplex virus.[59] So higher doses are required.

Dosage:

Adults: 800mg five times a day for 7 days.

Children: 20mg / kg every 6hours for 7 days

Intravenous Acyclovir is indicated in

a. Immunocompromised patients with disseminated infection
b. Patients with ophthalmic involvement.
c. Ramsay Hunt syndrome
d. Visceral dissemination
e. Patients with impaired intestinal function, intravenous route is preferred to ensure adequate drug level.

Dose:

In adults 10mg/kg body weight and 500mg/m^2 in children. Diluted with sterile water for injection and infused over one hour at every 8 hours for 7-10 days.

Complication:

Acyclovir is generally very well tolerated. The major risk is renal tubular crystallisation during rapid intravenous administration. In high dose and in dehydrated status caution must be exercised. CNS toxicity is uncommon. Thrombophlebitis is a known complication of infection due to high PH of the reconstituting solution (PH is 11). The plasma t1/2 is 2.5 hours requiring repeated administration but newer nanoparticle preparation has increased t1/2 and bioavailability. In future, Antiviral susceptibility testing allow selection of optimal drug.

Adverse drug reactions:

1. Interstitial nephritis
2. Obstructive nephropathy due to crystallisation of renal tubules
3. Tremors
4. Lethargy
5. Confusion
6. Seizures
7. Thrombophlebitis
8. Dermatitis
9. Fixed drug eruption
10. Elevated liver enzymes

Monitoring of therapy:

The dose should be adjusted for patients with creatinine clearance level less than 50ml/minute.

Valacyclovir:

Valacyclovir is a prodrug of acyclovir (L – valyl ester of acyclovir).

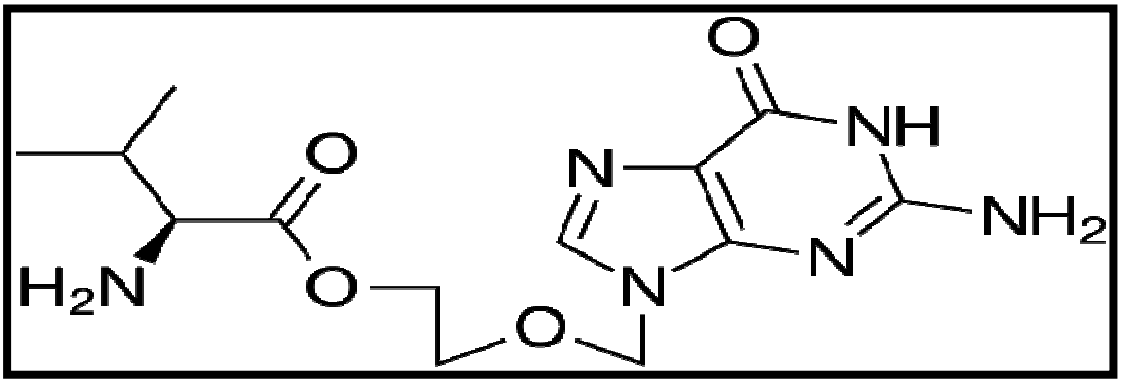


FIG: 8 STRUCTURE OF VALACYCLOVIR

Its oral bioavailability is 3 to 5 times that of acyclovir.[60]

Dose: 1 gm three times a day for 7 days.

Advantage:

Convenient dosing schedule and more rapid resolution of zoster associated pain.

Adverse reaction:

Most adverse effects are those that also occur with acyclovir.

- Severe and life threatening cases of thrombotic thrombocytopenic purpura and haemolytic uremic syndrome have been reported in AIDS and transplant recipient patients.
- Immediate hypersensitivity
- Symmetrical drug related intertrigenous and flexural exanthem.

Pregnancy: category - B

Famcyclovir:

It is a prodrug of penciclovir,[62] and has longer intracellular half-life of 7 hours.

Dose: 500mg three times a day for 7 days.

Adverse reaction:

Headache, nausea, diarrhoea, dizziness and leukocytoclastic vasculitis.

Precaution:

The dose should be reduced for patients with creatinine clearance less than 60ml/minute.

Foscarnet:

It is an analogue of inorganic pyrophosphate (Trisodium phosphonoformate). It does not require phosphorylation by thymidine kinase to get activated.

Mechanism of action:

It non-competitively inhibits viral DNA polymerase at the pyrophosphate binding site.[63]

Dose:

40 mg per kg intravenously every 8 hours, continued for at least 10 days or until lesions are completely healed.

Advantage:

Used in acyclovir, famcyclovir resistant cases of herpes zoster.

Adverse reaction:

- Electrolyte disturbances like hypokalaemia, hypocalcaemia, hypophosphatemia.
- Proteinuria
- Increased serum creatinine level
- Headache, fever
- Fatigue, seizures

- Reduced WBC count, haemoglobin
- Meatal irritation in males

Monitoring of therapy:

During drug administration close monitoring of renal function is needed.

Pregnancy: category - C

Vidarabine:

It is an adenosine analogue. It requires phosphorylation by host enzymes to be activated. In vivo Vidarabine is rapidly metabolized to hypoxanthine arabinoside by adenosine deaminase which reduce its antiviral activity. Dose related GI toxicities, acute neurotoxicities, leucopenia and thrombocytopenia limited the clinical use.[64]

Newer Drugs:

Birvudin:

Birvudin is a uracil analogue[65] with very high activity against VZV.

Dose:

It is effective in a single or twice daily oral dose (50 to 200mg) in immunocompetent adults. In immunocompromised patients high dose of 125mg tablet every 6 hours is required.

Sorivudine:

It is a uracil derivative with activity against VZV infection. It requires viral thymidine kinase for phosphorylation.

Anti-inflammatory Therapy:

CORTICOSTEROIDS:

Use of steroids in combination with antiviral therapy for herpes zoster remains subject of debate. Some studies provided evidence that combined regimen was found to accelerate the resolution of acute neuritis and improvement in quality of life and decrease in severity of PHN whereas randomised control trials[66] showed it has no effect on chronic pain. It is used in Ramsay Hunt syndrome, cranial nerve neuritis and ophthalmic zoster, as some believe that it may improve motor outcomes and acute pain in facial paralysis and cranial polyneuritis. The optimal duration of steroid therapy is not documented. The duration of therapy should not exceed beyond the period of antiviral therapy. The use of steroids for zoster without concomitant antiviral therapy is not recommended.

Dose:

Oral prednisolone 60mg/day for seven days then tapered to 30mg/day for next week and 15mg/day for the third week.

Analgesics:

Acetaminophen, NSAIDs (Non-steroidal anti-inflammatory drugs) and opioids used as analgesics.

Use of sub lesional anaesthesia, epidural blocks and sympathetic blocks with or without steroids are used to reduce NAP. Nerve blocks are considered if patients having very severe pain (unable to sleep or eat) and also in patients who have failed the standard therapies.

Treatment of Post herpetic neuralgia:

Pharmacotherapy for herpes zoster should accelerate healing, reduce the severity and duration of pain. There is currently no disease – modifying therapy for PHN, thus treatment is based on symptom control. Many patients with post herpetic neuralgia are elderly and have other diseases for which they are taking medication, particular caution is needed when prescribing medications for these patients. The most effective treatments result in clinically significant analgesia (e.g $\geq$ 50% pain relief) in fewer than half of patients.

Topical Therapy:

5% lidocaine:

Topical application of 5% lidocaine patch[67] produce significant relief in patients with PHN. It is not associated with systemic toxicity and

but mild redness, rash and allergic contact dermatitis may occur at the site of application.

Frequency of application: every 12 hours.

EMLA

Eutectic mixture of local anaesthetic preparation. It consist of 2.5% lignocaine and 2.5% prilocaine which reduces PHN.

Dose: 1-2gm of cream /10cm^2 of skin.

Adverse effects:

Skin blanching, erythema and oedema.

Topical capsaicin

Available as 0.025%, 0.075% patch or gel

It depletes the neurotransmitter substance P.

On application it first produces burning sensation (due to release of substance P) and then anaesthetic effect (depletion of substance P). To achieve anaesthetic effect it is applied 3 to 5 times daily.

Adverse reactions:

Pruritus, erythema, cough.

Botulinum Toxin:

Intradermal injection of botulinum toxin produces analgesic effect due to the release of acetylcholine which inhibit the release of substance P.

Dose: 15 units/10cm^2 of body surface area. It is diluted with 2% lignocaine and given intradermally.

Topical Aspirin tablets in chloroform and Doxepin Cream (5%).

SYSTEMIC THERAPY

Anti-convulsants, tricyclic antidepressants, are standard drugs used in management of PHN.

Anticonvulsants:

It is a membrane- stabilizing drugs.

Anticonvulsants like carbamazepine, sodium valproate, clonazepam, and Gabapentin are effective in shooting or lancinating pain.

Carbamazepine:

It stabilizes the inactivated state of voltage gated sodium channels and also a GABA agonist.

Dose: 100mg per day at bed time. It can be increased up to 200mg tds according to response.

Adverse effects:

Nausea, drowsiness, confusion, skin rashes aplastic anaemia, agranulocytosis.

Gabapentin:

It is a structural analogue of Gama amino butyric acid.[68] It exerts an effect on the presynaptic calcium channels of primary nociceptive endings.

Dose: 100- 300 mg per day given at night.

Adverse effects:

Dizziness, somnolence, headache.

Advantage: can be used in patients with coronary artery disease.

Pregabalin:

It is a structural derivative of GABA. It binds with high affinity to the α2-δ site of calcium channel subunit and reduce the release of neurotransmitters glutamate, norepinephrine and substance P. It has superior bioavailability.[69]

Dose: 100- 300 mg daily.

Adverse effects:

Dizziness, somnolence and peripheral oedema, headache, blurred vision.

Tricyclic antidepressants:

It blocks the reuptake of norepinephrine and serotonin. It decreases pain by inhibiting spinal nerves involved in pain perception. Amitriptyline, nortiptyline, desipramine are effective in post herpetic neuralgia.

Amitriptyline:

Dose: 10-25 mg per day at bed time.

Dose can be increased 25 mg every two to four weeks until response is adequate or maximum dose of 150mg per day.[70]

Adverse effect:

Dry mouth, drowsiness, confusion, constipation or urinary hesitancy.

Nortryptiline:

It is a metabolite of amitryptilne.[71] It has less anticholinergic effects than amitryptiline.

Dose: 10-25 mg per day at bed time. Can be given up to maximum dose of 150 mg per day.

Adverse effects:

Dry mouth, drowsiness, constipation or urinary hesitancy.

Desipramine:

It is a tricyclic antidepressant.[72]

Dose: 25 mg per day oral at bed time. Maximum dosage up to 150 mg per day.

Adverse effects:

Dry mouth, constipation, urinary retention, blurred vision.

Maprotiline:

It is a tetra cyclic antidepressant. It has strong effect as norepinephrine reuptake inhibitor with weak serotonin reuptake inhibition.[73]

Dose: 60mg/day.

Adverse effect:

Dizziness, drowsiness, somnolence, fatigue, dry mouth, heart block, arrhythmias, urinary retention.

Oxycodone:

Controlled release oxycodone,[74] an opioid analgesic (10mg every 12 hours) is an effective analgesic for the management of steady pain, paroxysmal spontaneous pain and allodynia.

Adverse effects: constipation, sedation, nausea.

Analgesics:

Aspirin and other nonsteroidal anti-inflammatory drugs are commonly used in patients with post herpetic neuralgia, but their value is limited. Tramadol[75], a centrally acting analgesic with opioid and non-opioid activities also effective in post herpetic neuralgia (maximum dose 600mg per day).

Anti-psychotics:

Fluphenazine, chlorprothixene and perphenazines are used with other drugs.

- Intradermal steroids, lignocaine and epinephrine injection.
- Inrathecal methyl Prednisolone[76] (3 ml of 3% lignocaine with 60mg of methyl prednisolone acetate).
- Sympathetic blocks (stellate ganglion or epidural) with 0.25% bupivacaine prevents or relieves post herpetic neuralgia. Epidural injection given at or just above the highest dermatome of the rash.
- TENS:

Transcutaneous electrical nerve stimulation may be helpful. It is the use of electrical currents produced by a device to stimulate the nerve for therapeutic purposes. The unit is usually connected to the skin using two or more electrodes.

TENS[76] is applied at high frequency (750HZ) with an intensity below motor contraction (sensory intensity) that produces motor contraction.

- Acupuncture[77]
- Spinal cord stimulators.
- Bio feed back
- Jaipur block[78]

This consists of local subcutaneous infiltration of 2% lignocaine, 0.5% bupivacaine, and 4mg/ml dexamethasone solution.[78] 28% of patients obtained complete relief from pain after a single injection, 57% after the second injection and 11% after third injection. The non responders were either aged over 60years or had pain lasting more than two years.

Modified Jaipur block:

It consists of local subcutaneous infiltration of 2% lignocaine, 0.5% bupivacaine and methyl prednisolone.[79]

SURGIAL PROCEDURES: (Neuroablation)

1. Division of dorsal root.
2. Rhizotomy (surgical separation of pain fibres).
3. Electrocoagulation of well-defined are of dorsal root.
4. Electrical stimulation of thalamus and spinal cord.
5. Anterolateral cordotomy

These procedures are not advocated nowadays due to limited efficacy and the high rate of morbidity.

Other treatment modalities:

Maintaining adequate nutrition is one contributing factor to ensuring healthy cell mediated immunity. Vitamin A deficiency has been

associated with increased susceptibility to numerous infection. So vitamin A is supplemented to augment CMI. Vitamin C, Vitamin E, lysine and zinc have shown potential benefit in HSV 1, 2 and herpes zoster.

Licorice[80] is one of the most widely used herbs which has anti-inflammatory, mucoprotectant and antiviral property. It inhibits viral growth and induces interferon production both in vivo and vitro.

Madonna lily (lilium candidum):

In northern Italy it is a traditional folk medicine.[81] It is fried in olive oil and applied externally as poultice on herpes zoster lesions.

Other natural therapy like reishi mushroom, clinacanthus nutans, honey, croton lechleri, aloe vera and St John's wort are used.

In south Indian rural areas and among illiterate people old methods like writing with saffron powder, applying neem paste and turmeric are followed. They used to come later with secondary infections and contact dermatitis.

PREVENTION:

Prevention of varicella

a. Varicella vaccine

b. Post exposure prophylaxis and infection control

a. Varicella vaccine:

The live attenuated VZV vaccine (Oka strain) is immunogenic and efficacious in protecting susceptible children against varicella.[82] Vaccinated children and adults developed varicella caused by wild type VZV at the rate of 1.1%-3% per year compared to an attack rate[83] of 8%-13% per year in unvaccinated children. The FDA approved Oka / Merck varicella vaccine[86] in 1995 and combination with MMR vaccine in 2005.

DOSE:

Two doses of 0.5 ml of varicella vaccine administered as subcutaneous injection, in the interval of 1 month – 3 months (< 12 yrs – 3 months, > 12 yrs – 1 month).

Indication of VZV vaccine for adults:

1. Health care workers
2. Household contacts of immunocompromised persons, including susceptible pregnant women

3. Non pregnant women of child bearing age
4. Adolescents and adults living with their children
5. International travellers.

Adverse reaction:

1. Skin rashes
2. Injection site reaction.

CDC recommend zoster vaccine to all immunocompetent people aged more 60 years including those who have had a previous episode of zoster. In March 2011, FDA approved the use of VZV vaccine in people aged more than 50-59 years.

Effective duration of this vaccination is not yet known. Benefits of vaccination persists at least 5 years after vaccination, through their magnitude decline somewhat over time.

Prevention of herpes zoster

1. Until the universal varicella vaccination greatly reduces the infection of wild type zoster virus, prevention should be aimed at preventing the reactivation and spread of latent wild type virus.

2. Long term viral suppression with acyclovir has been used in treatment in immunosuppressant patient during the period of activity and bone marrow suppression.
3. For the general population and elderly instead of viral suppression with acyclovir boosting of cell mediated immunity has been tried with live attenuated VZV vaccine which reduces the incidence and severity of post herpetic neuralgia.[87]
4. The FDA approved zoster vaccine for the prevention of zoster in elderly individuals (≥ 60 years) in 2006.

Contraindications for live vaccine:

1. Active tuberculosis
2. Leukaemia, lymphoma, and malignancy
3. AIDS with CDC count < 200 / mm^3
4. Long term immunosuppression (corticosteroid 20mg or more /day, prednisolone for 14 days or more, methotrexate >0.4mg/kg/week, azathioprine >3mg/kg/day, 6-mercaptopurine <1.5 mg/kg/day)

MATERIALS AND METHODS

This study was conducted from July 2015 to June 2016 in the Department of Dermatology and Venereology at Coimbatore Medical College Hospital after obtaining the ethical committee clearance.

Study design: Descriptive study

Study population:

One hundred and fifty consecutive herpes zoster cases attending the OPD and those referred from other departments were included in the study.

Informed consent in the regional language (Tamil) as well as in English was obtained.

Inclusion criteria:

Patients with zoster within 6 weeks duration of all age

Pregnant women

HIV positive persons

Exclusion criteria:

Patients who are unwilling to be included in the study.

Patients with zoster more than 6weeks duration attending for the first time.

Proforma was prepared which had the information about patient's (age, gender, occupation, and address) with history regarding prodromal symptoms, triggering factors and complications were noted. Past history of chicken pox was recorded.

Detailed clinical examination was done and the following information were entered.

- Dermatomal involvement
- Morphology of lesions
- Mucosal involvement.
- Lymphadenopathy

Investigations like Tzanck smear, CBC, RBS, HIV, urine routine were done in all patients. After confirming the diagnosis of herpes zoster, the patients were treated with acyclovir in standard dosage. (10-20mg/kg 5 times a day for 7 days).

The patients were followed up every week. The evolution of vesicles and presence of complications were recorded. All these data were tabulated, analysed and discussed.

OBSERVATION AND RESULTS

For this clinical study of herpes zoster a total of 150 cases were consecutively selected from outpatient clinic in Dermatology, Venereology and Leprology Department of Coimbatore Medical College hospital during the period from July 2015 to June 2016. All the 150 cases were studied and their varied clinical features and complications were noted and investigated.

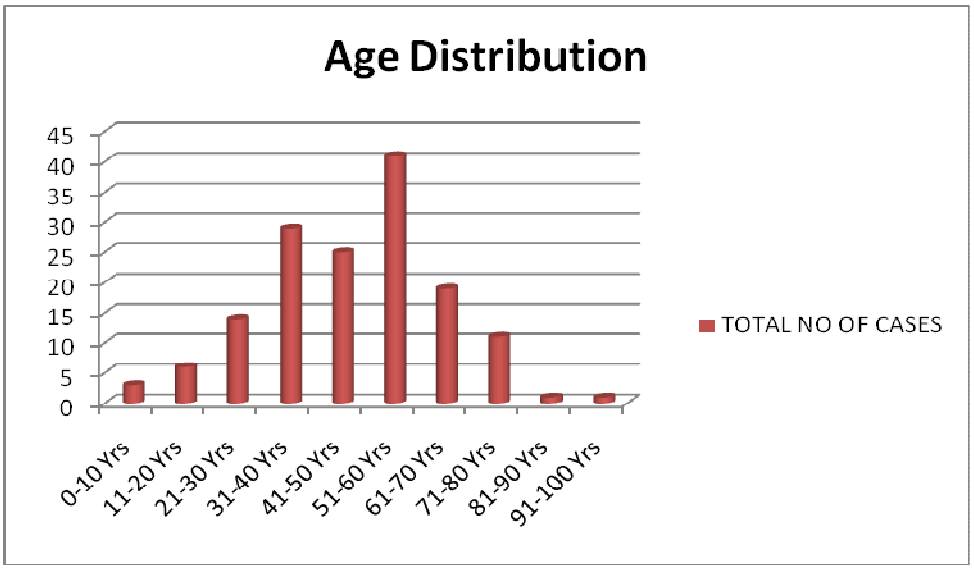
AGE DISTRIBUTION OF HERPES ZOSTER

In the present study majority of the patients i.e 41(27.33%) were in the 6th decade of life followed by 4th decade.

TABLE: 3 Age distribution of herpes zoster

S.no	Age group	Total no of cases	Percentage
1	1-10	3	2
2	11-20	6	4
3	21-30	14	9.3
4	31-40	29	19.33
5	41-50	25	16.66
6	51-60	41	27.33
7	61-70	19	12.66
8	71-80	11	7.33
9	81-90	1	0.66
10	91-100	1	0.66
	TOTAL	**150**	

Chart 1 : Age distribution of herpes zoster



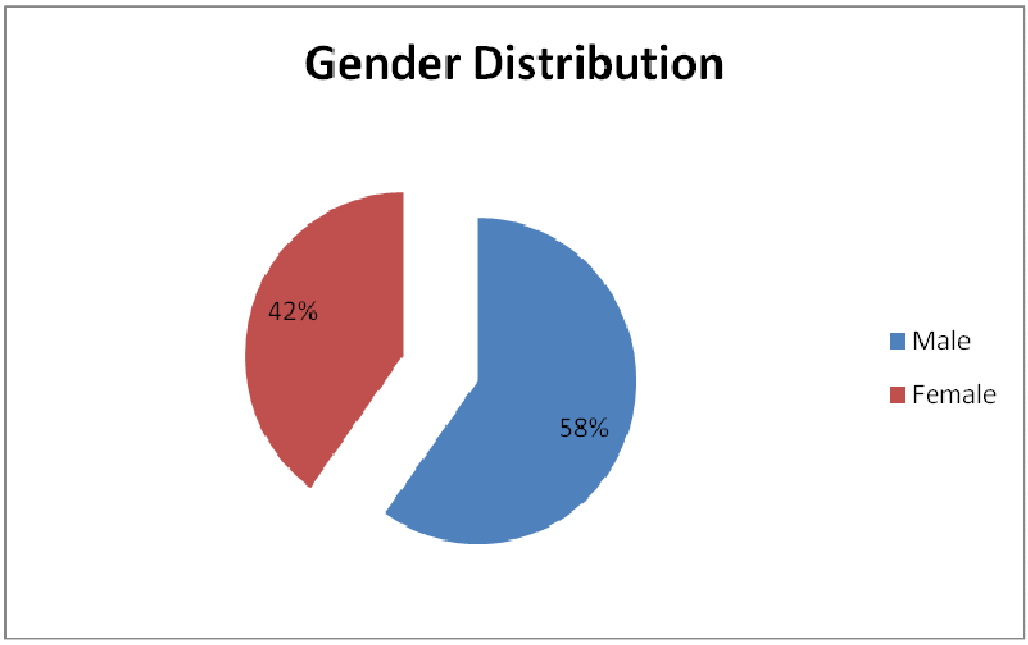
GENDER DISTRIBUTION

Out of 150 cases 87 were males and 63 were females with gender ratio of 1.5:1.

TABLE 4 : GENDER DISTRIBUTION

Sex	No. of Cases	Percentage
Male	87	58
Female	63	42
Total	**150**	

Chart 2 : Gender Distribution



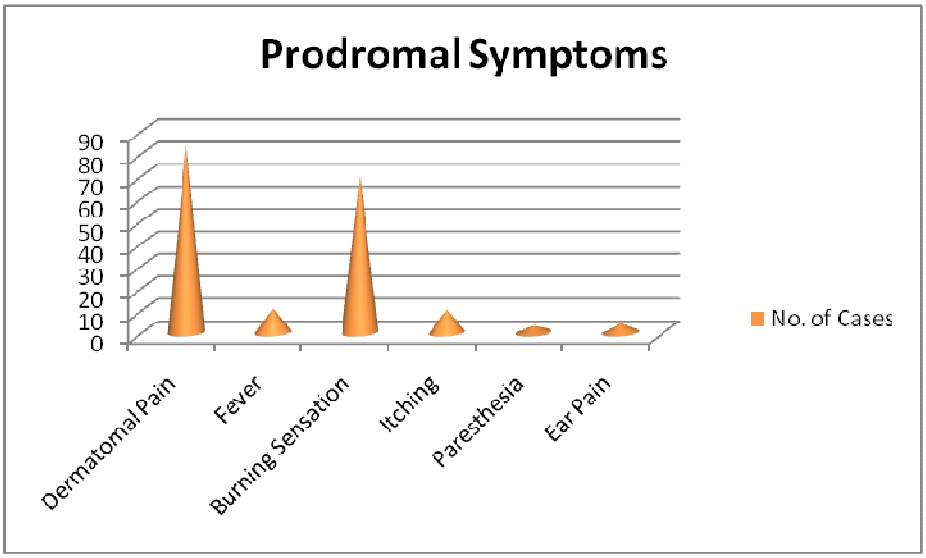
PRODROMAL SYMPTOMS

Out of 150 cases 126 cases presented with prodromal symptoms. Dermatomal pain (66%) and burning sensation 55.5% were the major presenting symptom. Among 126 cases many had more than one prodromal symptoms.

Table 5 : Prodromal Symptoms

S.No.	Prodromal Symptoms	No. of Cases	Percentage
1	Dermatomal Pain	84	66
2	Fever	11	8.7
3	Burning Sensation	70	55.55
4	Itching	10	7.93
5	Paresthesia	3	2.38
6	Ear Pain	4	3.17

Chart 3 : Prodromal Symptoms



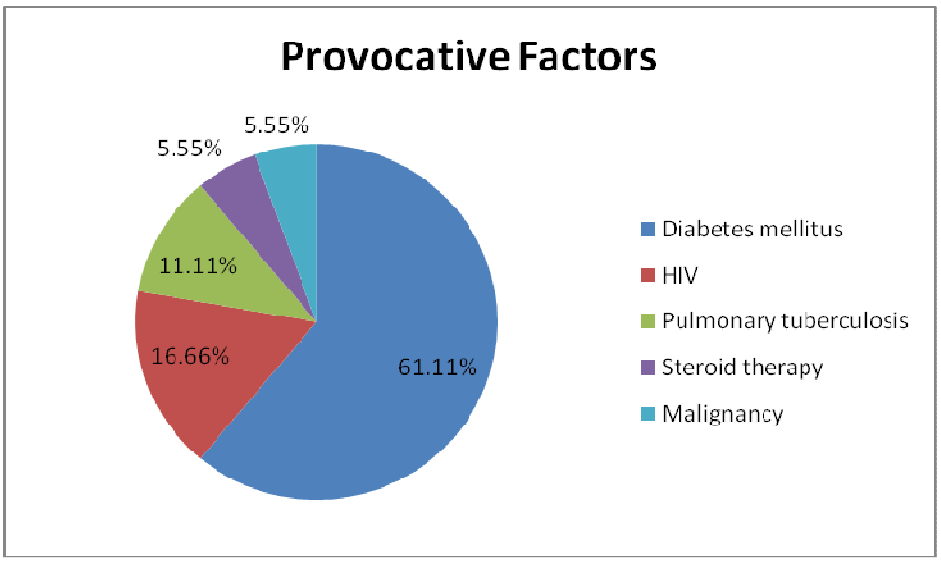
PROVOCATIVE FACTORS

Among the 150 cases 18 cases had provocative factors like diabetes mellitus 61.1% (11cases), HIV 16.6 % (2 male and one male child), pulmonary tuberculosis 11.1% (2cases), malignancy 5.55% (carcinoma stomach) and steroid therapy 5.5%.

Table 6 : Provocative factors

S.No.	Provocative Factors	Male	Female	Total no. of Cases	Percentage
1	Diabetes mellitus	7	4	11	61.11
2	HIV	3	0	3	16.66
3	Pulmonary tuberculosis	1	1	2	11.11
4	Steroid therapy	1	0	1	5.55
5	Malignancy	1	0	1	5.55
	Total	**13**	**5**	**18**	

Chart 4 : Provocative factors



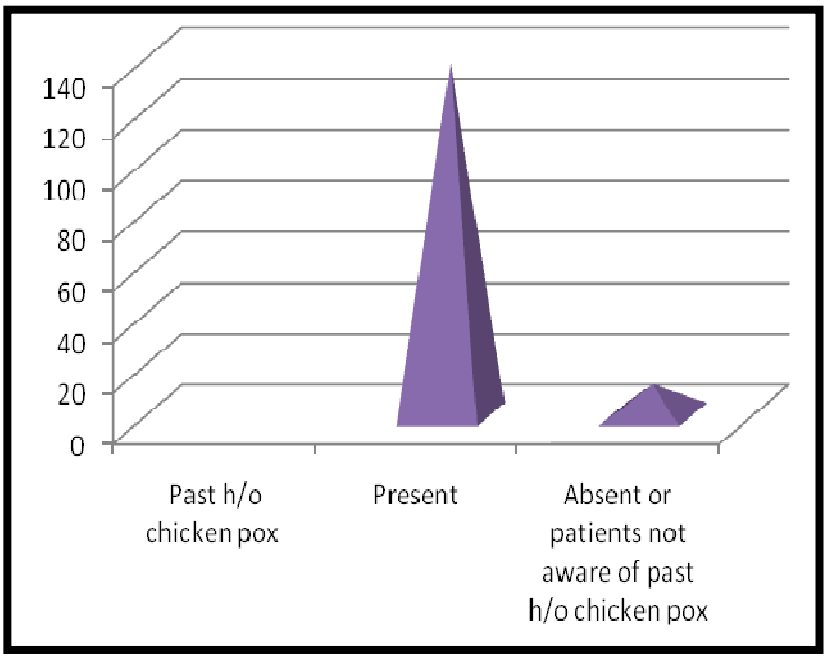
PAST HISTORY OF CHICKEN POX

The below table shows 138 cases had past history of chicken pox and 12 cases had absent or not aware of past history of chicken pox.

Table 7 : Past history of chicken pox

Past h/o chicken pox	Present	Absent or patients not aware of past h/o chicken pox
	138	12

Chart 5 : Past history of chicken pox



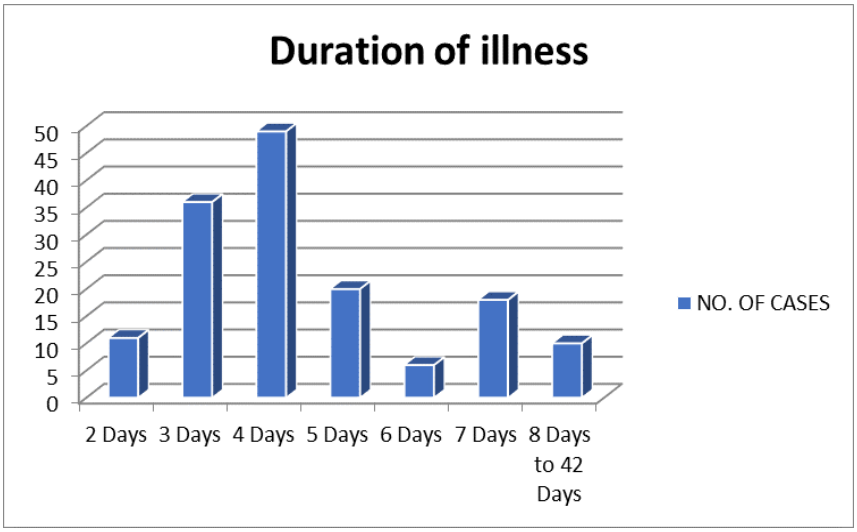
DURATION OF ILLNESS AT THE TIME OF PRESENTATION

In this study maximum number of cases (76%) presented between second and fifth day of prodromal symptoms. Among 76% of cases 7.33% presented on second day which was the earliest presentation.

Table 8 : Duration of illness

s.no	Duration of illness	No. of cases	Percentage
1	2 Days	11	7.33
2	3 Days	36	24
3	4 Days	49	32
4	5 Days	20	13.33
5	6 Days	6	4
6	7 Days	18	12
7	8 Days to 42 Days	10	6.66

Chart 6 : Duration of illness



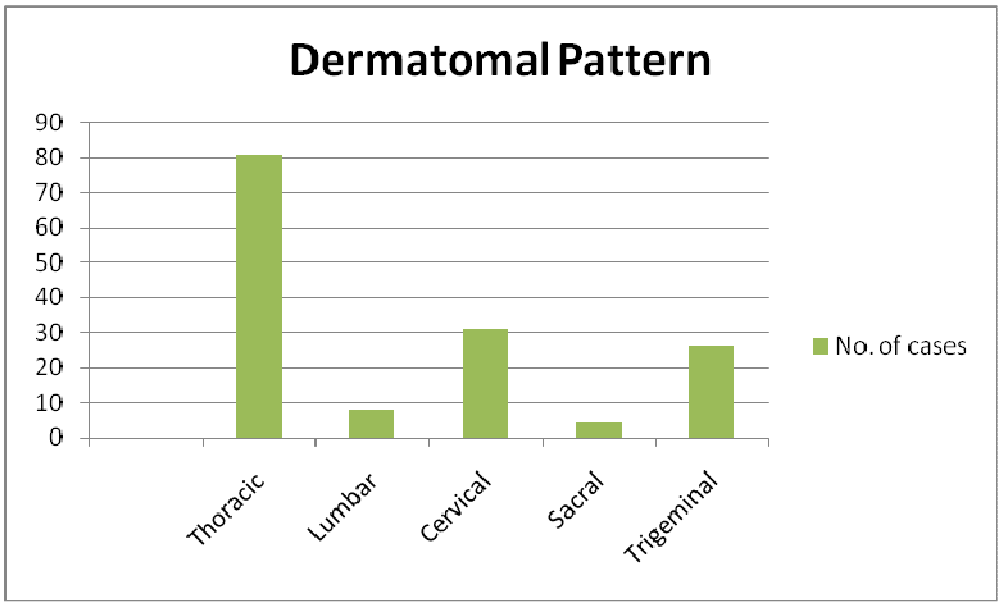
PATTERN OF DERMATOMAL INVOLVEMENT

Thoracic dermatome was the most commonest dermatome involved (54%) followed by cervical (20.6%), trigeminal (17.33%), lumbar (5.33%) and sacral (2.66%). The pattern of dermatome involvement was almost similar in both gender.

Table 9 : Pattern of dermatomal involvement

S.No	Dermatome	Gender		No. of cases	Percentage
		Male	Female		
1	Thoracic	49	32	81	54
2	Lumbar	2	6	8	5.33
3	Cervical	19	12	31	20.66
4	Sacral	2	2	4	2.66
5	Trigeminal	14	12	26	17.33
	Total Cases	**86**	**64**	**150**	

Chart 7 : Pattern of dermatomal involvement



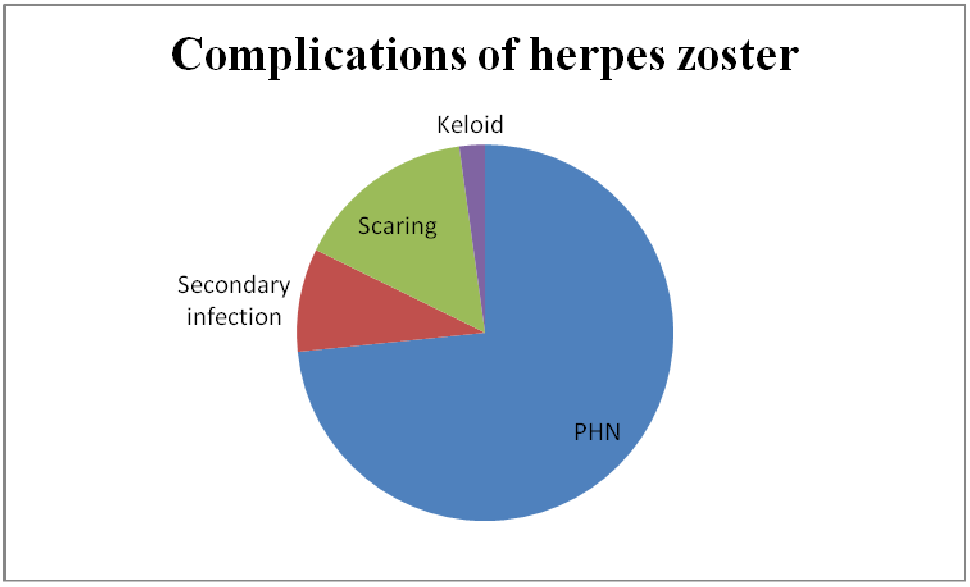
COMPLICATIONS OF HERPES ZOSTER

Out 150 cases 45 cases had complications**.** The most common complication was post herpetic neuralgia (22%).

Table 10 : Complications of herpes zoster

S.No.	Complications	Male	Female	Percentage
1	PHN	19	14	22
2	Secondary infection	2	2	2.66
3	Scaring	5	2	4.66
4	Keloid	0	1	0.66
	Total	**26**	**19**	

Chart 8: Complications of herpes zoster



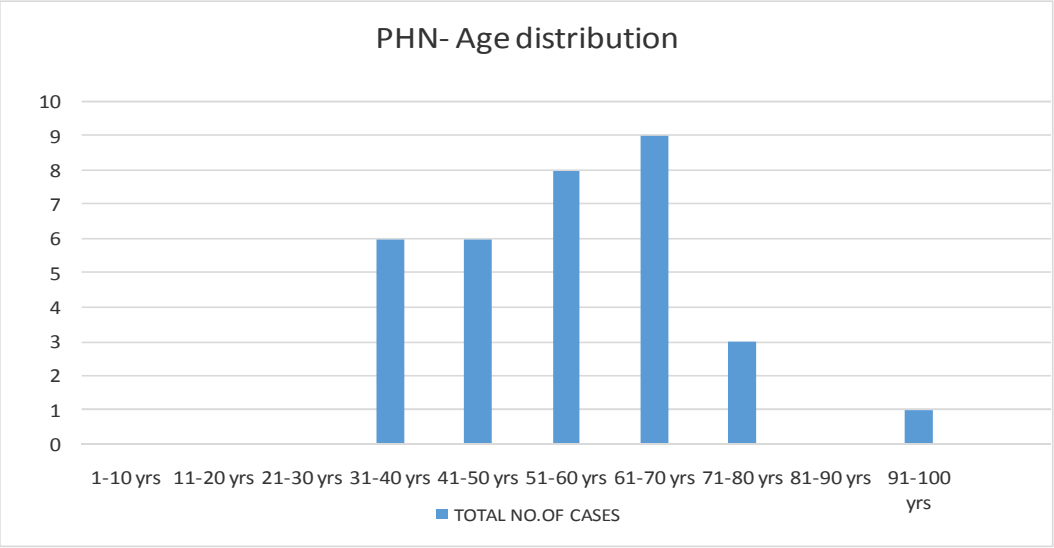
PHN – AGE DISTRIBUTION

Post herpetic neuralgia was the commonest complication 22% (33 cases) seen in our study. The commonest age group affected in our study belonged to 61-70 years.

Table 11: PHN – Age distribution

S.no	Age group	Male	Female	Total	Percentage
1	1-10	-	-	-	-
2	11-20	-	-	-	-
3	21-30	-	-	-	-
4	31-40	4	2	6	18.88
5	41-50	5	1	6	18.88
6	51-60	5	3	8	24.24
7	61-70	2	7	9	27.77
8	71-80	2	1	3	9.09
s9	81-90	-	-	-	-
10	91-100	-	1	1	3.03
	TOTAL	**18**	15	33	

Chart 9 : PHN – Age distribution



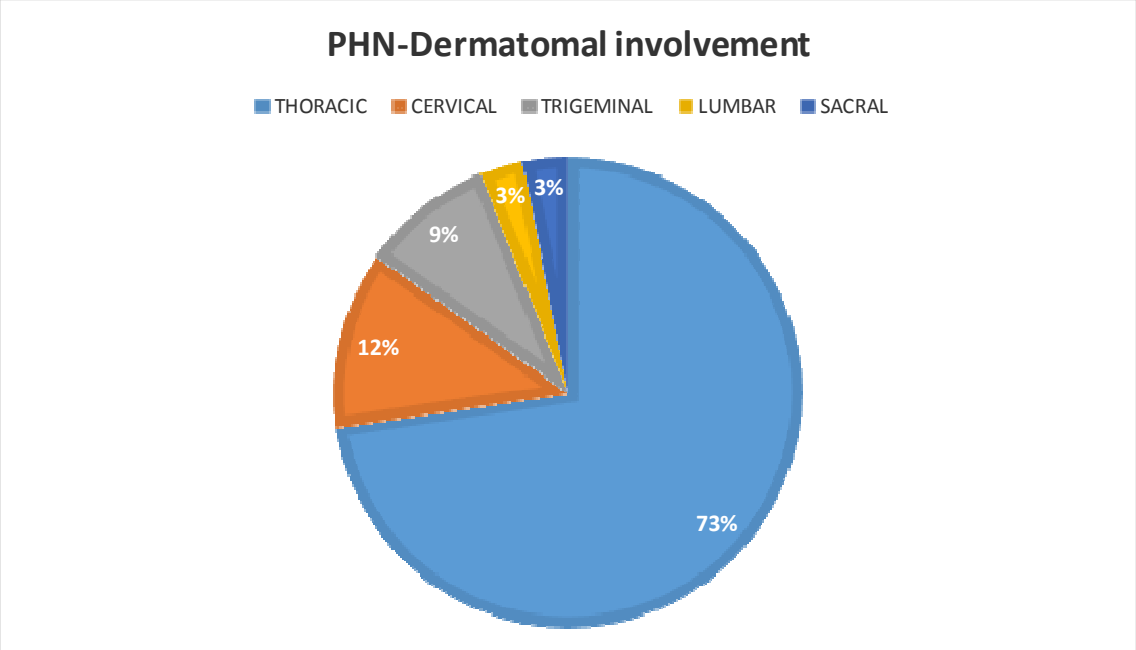
PHN – Dermatomal involvement

33 cases of post herpetic among neuralgia 24 cases had thoracic involvement followed by cervical dermatome.

Table 12 : PHN – dermatomal involvement

Dermatome	Male	Female	Total
Thoracic	14	10	24
Cervical	1	3	4
Trigeminal	3	-	3
Lumbar	1	-	1
Sacral	-	1	1

Chart 10 : PHN – dermatomal involvement



DISCUSSION

Herpes zoster is caused by the reactivation of latent varicella zoster virus. In general population, the lifetime incidence of herpes zoster is 10-20%, which increases with age.

Post herpetic neuralgia is a debilitating complication of zoster. It is defined as persistence or recurrence of pain for more than a month after onset of zoster. The pain results in large part from damage to the sensory nerves, causing neuropathic pain. It is not uncommon for the pain of PHN to interfere with sleep and recreational activities.

In our study maximum number of cases belong to the age group of 50-60 years (27%) followed by 31- 40 years (19.33%). This is comparable to Toyama and Shiraki[88] study which reported higher rate of occurrence in individuals aged 50-70 years.

The youngest case and oldest case reported in our study were two years and 96 years respectively.

Out of 150 cases 87 cases were male and 63 cases were female, with the sex ratio of 1.5:1, which is in concordance with other Indian studies (Abdul et al[89] and Agarwal SK et al[90]) but in contrast to western studies where there is no sex preponderance.

Our study showed that 18 cases (12%) had provocative factors for developing herpes zoster. Among them diabetes mellitus was common and constituted (61.1%) (11cases), followed by HIV 16.66 % (3 cases) and pulmonary tuberculosis 11.11% (2 cases). One case of malignancy and one patient on steroid therapy were reported. This is similar to Frahang Babamahmoodi et al[91] study.

One thirty eight cases (93%) had past history of chickenpox and 12 cases were either not aware or not had chicken pox at all. This is similar to Frahang Babamahmoodi et al[91] study, where 95% had past history of chicken pox.

In this study maximum number of cases (76%) presented to OPD between 2nd and 5th day of prodromal symptoms. out of 96 cases 7.33% presented on 2nd day.

The prodromal symptoms like fever, burning pain were seen in 126 Cases (84%). Among them many had more than one prodromal symptoms. Dermatomal pain (66%) and burning sensation (55.5%) were the major presenting symptoms. This is in concordance with Abdul et al[89] study.

The commonest dermatome involved in herpes zoster was thoracic (54%). The next common involvement was cervical (20.66%) followed

by trigeminal (17.33%), lumbar (5.33%) and sacral (2.66%) which is comparable with the Shegal et al[92], Chaudhary et al[93] and Nigam et al[94] studies.

In our study out of 150 cases 45 cases had developed complications. Post herpetic neuralgia was the most common complication reported in our study 33 cases (22%) and was commonly seen in 7th decade. Among 33 cases 24 had thoracic involvement followed by cervical dermatome. R. E. Hope-Simpson[13] study also reported PHN as the commonest complication with predominant thoracic dermatomal involvement.

Some of the interesting observations we made in our study were

1. One HIV positive child with sacral dermatomal involvement.
2. Keloid in the healed zoster lesions.
3. Twenty six cases of trigeminal zoster.

CONCLUSION

The following conclusion can be drawn from the present study

1. Highest incidence of the disease was seen in the 6th decade of life.
2. There was a male predominance with sex ratio of 1.5:1
3. Almost about two third of patients had prodromal symptoms whereas most of patients presented with classical lesions.
4. Most common presenting symptom was prodromal pain.
5. Constitutional symptoms were noted in majority of cases and were in younger age group.
6. Thoracic segment was the most commonly involved dermatome among the others.
7. Unidermatomal involvement was seen in most of the patients.
8. Diabetes mellitus, hypertension and pulmonary tuberculosis were the systemic diseases associated with herpes zoster.
9. Ninety two percent of the patients gave strong history of chicken pox in the past as others did not remember to have had chicken pox or probably in those chicken pox was very mild as it is so when it occurs in the first decade of life.

POST HERPETIC NEURALGIA:

Post herpetic neuralgia was the commonest complication (22 %) and the incidence of PHN increased with increasing age. The other complication seen were secondary bacterial infection and scarring.

PHN was commonly seen in thoracic dermatome as the most common dermatome involved in zoster itself is thoracic. Early initiation of antiviral drugs decreases the incidence of PHN. Anticonvulsants, antidepressants, topical and above all reassurance improves the quality of life of people with PHN. Steroid in HZ and PHN is the subject of debate.

Recent milestone in HZ and PHN is the vaccination and when given in elderly >60 yrs reduces the morbidity and improves the social wellbeing of geriatric individuals.

Limitations:

We were not able to find the incidence of herpes zoster and post herpetic neuralgia in the community as our study was a hospital based. The follow up period in our study was 3 months only. The longer follow up could have provided better picture about the course of PHN.

EVOLUTION OF HERPES ZOSTER

Fig 1 : Erythematous Papules

Fig 2 : Vesicles

Fig 3 : Bullae with crust

Fig 4 : Erosion

DERMATOMAL INVOLVEMENT

Fig 5 : Cervical Dermatome

Fig 6 : Thoracic Dermatome

Fig. 7 : Lumbar Dermatome

Fig. 8 : Sacral Dermatome

Fig. 9 : Trigeminal Dermatome : Opthalmic branch

Fig. 10 : Trigeminal Dermatome : Maxillary branch

COMPLICATION OF HERPES ZOSTER

Fig. 11 : Secondary Infection

Fig. 12 : Dyspigmentation

Fig. 13 : Scarring

Fig. 14 : Keloid

EXTREMES OF AGE

Fig 15 : 2 yrs of Age

Fig 16 : 96 yrs of Age

BIBLIOGRAPHY

1. Heininger U, Seward JF. Varicella. Lancet 2006 ; 368:-1365-76
2. Gershon AA, Steinberg SP, Gelb L. Clinical reinfection with vareicella-zoster virus. J infect Dis; 1984; 149: 137-142
3. Juhl-Jenson BE. The natural history of shingles. Events associated with reactivation of varicella zoster virus. J.R CollGenPract 1970; 20: 323-7
4. JE Gordon. Chickenpox: an epidemiological review. Am J Med Sci 244:362-389,1962
5. AA Gershon SJ Silverstein. Varicella- zoster virus In; DD Richman,RJWhitely,FG Hayden, eds. Clinical, Virology.New York: Churchill Livingstone,1997, pp421-444
6. Steiner P. ZurInokulation der varicelleu. Wein Med Wochenschr. 1875; 25:306.
7. Von Bokay J. Uber den aetiologischen zusammenhang dervarizellen mit gewissen fallen von herpes zoster Wien Wochenschr, 22: 1323, 1909.
8. Kundratitz K. Experimentelle ubertragwagen von herpes zoster auf menschen und die beziehungen von herpes zoster varicelleu. Z Kinderheilkd 1925; 39: 379..

9. Lipschutz B. Untersuchungenuber die etiologieskrankheiten der Herpes gruppe (Herpes zoster, Herpes genitalis, Herpes febrilis) Arch DermatolSyph. 1921: 136:
10. Garland J. Varicella following exposure to herpes zoster. Engl J Med. 1943; 228:336.
11. Weller TH, Witton HM. The etiologic agent of Varicella and herpes zoster: Serologic studies with the viruses as propagated in vitro. J Exp Med. 1958; 228; 336-337.
12. Grossman MC and Silvers DN. The Tzanck Smear: Can Dermatologists accurately interpret it? Journal of Americal Academy of Dermatology. 27: 403-5, September 1992.
13. Hope- Simpson RE: The nature of herpes zoster: a long term study and a new hypothesis. Proc R Soc Med 58: 9, 1965.
14. Loparev VN, Gonalez A, Deleon-carnes M et al Global identification of three major genotypes of varicella-zoster virus:longitudinal clustering and strategies for genotypingJ virol2004; 78:8349-58
15. Almeida JD. Howatson AF. Williams MG. Morphology of Varicella (Chickenpox) virus. Virology. 1962; 16: 353.
16. Choopw Donahue JG,Manson JE et al. the epidemiology of varicella and its complications. J infect dis 1995;172:706-12
17. Brisson M, Edmunds WJ.epidemiology of varicella- zoster virus in England and Wales.j med virol2003;70 suppl 1:S9-14

18. Cohen JI, Straus SE, Arvin AM: V aricella-zoster virus replication, pathogenesis and management. In: Fields Virology, Vol. 2, 5th edition, edite by D Knipe, X Howley,eds. Philadelphia, Lippincott Williams & Wilkins, 2007,p. 2744

19. Arvin AM: Humoral and cellular immunity to varicellazoster virus: An overview. J Infect Dis 197:S58, 2008

20. Kost RG, Straus SE. Postherpetic neuralgia—pathogenesis, treatment, and prevention. NEngl J Med 1996; 335: 32–42.

21. William D James timothy G. berger ,dirk M. elston, Andrews dis of the skin chap, eleventh edition page 374.

22. Kenneth E. Schmader and Michael N. Oxasm varicella and herpes zoster, Fitspatricks, chapter 194, vol11 eight edition page 2387.

23. Kenneth E. Schmader and Michael N. Oxasm varicella and herpes zoster, Fitspatricks, chapter 194, vol11 eight edition page 2386.

24. Oxman MN and Rhoda Alani. Varicella and herpes zoster. In: Dermatology in General Medicine, 4th Edition. Thomas B. Fitzpatrick et al, Eds. Newyork: Mc Graw-Hill Incl., 1993, Vol.2: 2543-2572.

25. Neal Penneys. Diseases caused by viruses. In: levers Histopathobhy of the skin, Eighth edition. David Elder et al, Eds. Philadelphia: Lippincott-Raven publishers, 1997. Page 569-589.
26. Erhard H, Runner Tm, kreinkamp M et al: Atypical varicellazoster virus infection in an immuno compromised patient: result of a virus induced vasculitis. J Am Acad Dermatology 1995: 32: 908-911.
27. Nikkels AF. SnoeckR, Rentier B, Pierard GE, Chronic verrucous vermicelli zoster virus skin lesions, Clinical, histological, molecular and therapeutic aspects. clin Exp. Dermatol 1999:24: 346-353.
28. Levin MJ et al: Decline in varicella-zoster virus (VZV) specific cell-mediated immunity with increasing ageand boosting with a high-dose VZV vaccine. J Infect Dis 2003 ;188:1336 – 1344.
29. J.C.Sterling, viral Infection, Rook's Text book of dermatology, eighth edition, Vol II : 2010; 33: Page 33.25.
30. Rifkind D. The activation of varicella -zoster viral infections by immunosuppressive therapy. J Lab clin Med 1966; 68:463-74.
31. Umesh RE. Herpes zoster ophthalmicus and HIV infection inNigeria. Int J STD AIDS 1998:9: 476-479.
32. Palexas GN, Welsh NH, Herpes zoster ophthalmicus an early point to HIV-I positivity in young African patients. Scand J Immunol supple 1992, 11: 67-68.

33. Marsh RJ, Dulley B, Kelly V. External ocular motor palsies in ophthalmiczoster:a review. Br J Ophthalmol1977; 61: 677–82.

34. Tomkinson A, Roblin DG, Brown MJ. Hutchinson's sign and its importance in Rhino logy, Rhino logy 1995: 33(3):180-182.

35. Nally FF, Ross IH. Herpes zoster of oral and facial structures. Reports of 5 cases and discussion. Oral surg. Oral med, oral pathol .1971: 32:34.

36. Aleksic SN, Budzilovich GN, Lieberman AN. Herpes zoster oticus and facial paralysis (Ramsay Hunt syndrome). Clinico-pathologic study and review of literature. J NeurolSci1973; 149-59.20

37. Sweeney CJ, Gilden DH. Ramsay Hunt syndrome. J NeurolNeurosurg Psychiatry 2001; 71: 149–54.

38.. Landthaler M, Heuser M. ParalytischeBauchwandherniebei zoster. Hautarzt 1979; 30: 432-3.

39. Sellitti TP, Huang AJ, Schiffman J et al. Association of herpes zoster ophthalmicus with acquired immunodeficiency syndrome and acute retinal necrosis. Am J Ophthalmol1993; 116: 297–301.

40. Nikkels AF, Snoeck R, Rentier B et al. Chronic verrucous varicella zoster virus skin lesions: clinical, histological, molecular and therapeutic aspects. ClinExpDermatol1999; 24: 346–53.

41. Mc Kinlay WJD; Herpes zoster in pregnancy. Br Med J 1980; 280: 561.

42.. J.E.Banatvala; Viral Infections in Pregnancy. In Oxford Textbook of Medicine, 3rd edition. Leadingham JGG, Weatherall DG and Warell DA, Eds. Oxford: Oxford University Press, 1996, p 1775-1784.

43. Baba K, Yabuuchi H, Taka Hashi M et al; Increased incidenceof herpes zoster in normal children infected with varicellazoster virus during infancy: community based follow upstudy. J Paediatric 108: 372: 1986.

44. Robillard RB, Hil singer RL, Adout K. Ramsay- Hunt facial paralysis: clinical analysis of 185 patients. Otolaryngology, Head and neck surgery 1986: 95: 292-297.

45. 17 Marsh RJ, Dulley B, Kelly V. External ocular motor palsies in ophthalmic zoster: a review. Br J Ophthalmol1977; 61: 677–82.

46. W R McCormic,RLRodnitzky, SS S chocherjr AP McKee.Varicella zoster encephalomyelitis. Arch Neurol 21:559-570, 1969.

47. Heiberg – Actaotol – laryngol. 1961; 53:536, (report of case of glossopharyngeal).

48. Mc Govern – Southern Med. J. 1951; 44:137, (vagal type).

49. Akiyama N. Herpes zoster infection complicated by motor paralysis. J Dermatol2000; 27: 252–7.

50. Fugelso PD, Reed WB, Newman SB et al. Herpes zoster of the anogenital Area affecting urination and defaecation. Br J Dermatol1973; 89: 285–8.

51. JG Bullowa, SM Wishik, complications of varicella: I their occurrence among 2,534 patients. Am J Dis Child 49;9 23-926. 1935.

52. Yoong MF, Blumbergs PC, North B: Primary (granulomatous angiitis of the central nervous system with multiple neurysms of spinal arteries. J Neurosurg, 79: 603, 1993.

53. Huang CW, Tu ME, Wu YH et al. Isotopic response of fungal granuloma following facial herpes zoster infections—report of three cases. Int J Dermatol2007; 46: 1141–5.

54. Ruocco E, Baroni A, Cutri FT et al. Granuloma annulare in a site of healedherpes zoster: Wolf's isotopic response. J EurAcad Dermatol Venereol 2003;17:686–8.

55. CJ JayaramPaniker, Herpes viruse. In: Anatharaman and Paniker's Textbook of Microbiology, 7th Edition, page: 478-481.

56. Nahass GT, Goldstein BA, Zhu WY, et al. Comparison of Tzanck smear, viral culture and DNA diagnostic methods in detection of herpes simplex and Varicella zoster infection. JAMA 268:2541-2544, 1992.

57. StepenE.Straus, Kenneth E. SChmader, Michael. N Oxman varicella &Herper Zoster. In Fitzpatrick's Dermatology ingeneralmedinice sixth edition, Irwin m. freed berg, ArthunZ. Eisen, Klaus wolff, et al: eds. New yosk: Mc Graw- hill, 2003, vol 2: page 2070-2084.

58. Wallace MR et al: Treatment of adult varicella with oral acyclovir: A randomized, placebo-controlled study. AnnIntern Med 117:358, 1992

59. Klassen TP et al: Acyclovir for treating varicella in otherwise healthy children and adolescents. Cochrane DatabaseSyst Rev (4):CD002980, 2005

60. Beutner KR: Valaciclovir; A review of its antiviral activity, Pharmacio kinetic properties, and clinical efficacy. Antiviral Ref 28; 281, 1995.

61. Beutner KR et al. valacyclovir compared with acyclovir for improved therapy for herpes zoster in immunocompetent adults. Antimicrob agent's chemother 39:1546, 1995.

62. Vere Hodge RA: Famciclovir and penciclovir. Antiviral chemche mother 4:67, 1993.

63. Crumpacker CS: Mechamism of action of foscarnet against viral polymerases. Am J Med 92 (supp 2A): 2A, 1992

64. Sharon safrin and chambers HF. Antiviral agents. In: Basics and clinical pharmacology, seventh edition. Bertram G kartzung (editor). San Francisco. Prentice –Hall International, 1997.P 788-800.

65. GnannJw Jr. New antivirals with activity against VZV. Annals of Neurology. 35 (supple): s 69-72, 1994.

66. Whitley RJ et al: Aciclovir with and without prednisone for the treatment of herpes zoster: A randomized, placebocontrolled trial. The National Institute of Allergy and Infectious Diseases collaborative Antiviral study Group. AnnInternal Med 125: 376, 1996.

67. Devers A, Galer BS. Topical lidocaine patch relieves a variety of neuropathic pain conditions: an open label study. Clin J pain 2000; 16: 205-8.

68. Rowbotham M, Harden N, Stacy B et al. Gabapentin for the treatment of postherpetic neuralgia: a multicentre double-blind, placebo-controlled study. JAMA 1998; 280: 1837–42.

69. Gilron I, Flatters SJL. Gabapentin and pregabalin for the treatment of neuropathicpain: a review of laboratory and clinical evidence. Pain Res Manage 2006;11(Suppl. a): 16A–29A.

70. Watson CP, Evans RJ, Reed K et al. Amitriptyline versus placebo in post-herpetic neuralgia. Neurology 1982; 32: 670–3.

71. Watson CP, Vernich L, Chipman M, Reed K. Nortriptyline versus amitriptylineinpostherpetic neuralgia: a randomized trial. Neurology 1998; 51: 1166–71.

72. Kishore-Kumar R, Max MB, Schafer SC et al. Desipramine relieves postherpetic neuralgia. ClinPharmacolTher1990; 47: 305–12.

73. Watson CPN, Chipman M, Reed K et al. Amitriptyline versus maprotiline in post herpetic neuralgia: a randomized, double-blind crossover trial. Pain 1992; 48:29–36.

74. Watson CP, Babul N. Efficacy of oxycodone in neuropathic pain: a randomized trial in postherpetic neuralgia. Neurology 1998; 50: 1837–41.

75. Gobel H, Stadler T. Treatment of post herpes zoster pain with treatment of post herpes zoster pain with tramadol. Drugs 1997; 53:349.

76. Yamashiro H, Hara K, Gotoh Y. Relief of intractable post-herpetic neuralgia with gasserian ganglion block using methyprednisolone acetate and with TENS.Masui1990; 39: 1239–44.30

77. Lewith GT, Field J, Machin D. Acupuncture compared with placebo in postherpetic neuralgia. Pain 1983; 17: 361–8.

78. Rishi Bhargava et al: Jaipur block in PHN. Internationaljournal of Dermatology. 37:405-408, 1998.

79. Modified Jaipur block, Int J dermatol 2011 nov;50(11):1417-20.

80. Baba M, Shigeta S. Antiviral activity of glycyrrhizin against varicella – zoster in vitro antiviral Res 1987;7;99-107.

81. Pieroni A. Medicinal plants and food medicines in the folk traditions of the upper Lucca province, Italy. J Ethnopharmacol 2000;17;235-273.

82. Seward JF et al: Varicella disease after introduction of varicella vaccine in the United States, 1995–2000, JAMA 287:606, 2002

83. Jumaan AO et al: Incidence of herpes zoster, before and after varicella-vaccination-associated decreases in the incidence of varicella, 1992–2002. J Infect Dis 191:2002, 2005

84. Robinson DM, Perry CM, Zoster vaccine live (Oka Merck), Drugs Aging. 2006, 23 (6) 525 - 31.

85. Garner JS: Guideline for isolation precautions in hospitals. The Hospital Infection Control Advisory Committee. Infect Control HospEpidemiol 17:53, 1996

86. Bolyard EA et al: Guidelin for Infection Control in Health Care Personnel. AJIC26:289, 1998.

87. Oxman MN et al: A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. NEngl J Med352:2271, 2005.

88. Toyama N, Shiraki K. society of the Miyazaki prefecture Dermatologist. Epidemiology of herpes zoster and its relationship to varicella in Japan: a 10 year survey of 48,388 herpes zoster cases in Miryazaki prefecture. J Med Virol.2009;81:2053-2058.

89. Abdul Latheef EN, PavithranK.Herpes zoster: A clinical study in 205 patients Indian J dermatol.2011 sep-oct; 56(5): 529-532.

90. Aggarwal SK, Radhakrishnan S, A Clinic-epidemiological study of herpes zoster, medical Journal armed forces India (2015).

91. FarhangBabamahmoodi et al ,clinical manifestations of Herpes zoster, Its Comorbidities, and Its complications in North of Iran from 2007-2013, Hindawi Publishing corporation Neurology Research International volume 2015,Article ID 896098, 4 pages.

92. Sehgal VN, Rege VL, Kharangate VN, Reys M. The natural history of herpes zoster. Indian J DermatolVenereolleprol 1976; 42(2): 86-89.

93. Chaudry SD, Dashore A, Pahwa US. A clinico-epidemiologic profile of herpes zoster in North India. Indian J DermatolVenereolLeprol 1987; 53: 213-216.

94. Nigam P. Tandon VK, Kumar R, Sahai I, Agrawal LP. Herpes zoster- A clinical study. Indian J DermatolVenereol 1972; 38(4) 152-155.

PROFORMA

Name : Date :

Age :

Sex :

Address :

Occupation :

Phone No. :

PRESENTING COMPLAINTS:

H/O. PRESENT ILLNESS

H/o. vesicles - onset, progression, duration

H/o. Pain

Nature of pain:

- Lancinating
- Shooting
- Burning
- Throbbing

H/o. Paraesthesia

H/o. Fever, Malaise

H/o. itching, tingling, numbness over the involved site

H/o. Pain,Photophobia, swelling, watering in eye

H/o. Headache

H/o. Toothache

H/o. ear pain

H/o. Tinnitus and giddiness

H/o. Difficulty in urination / defecation

Other complaints

PAST HISTORY

H/o. Varicella

H/o. Diabetes, TB

H/o. Recurrent Zoster

H/o. malignancy

TREATMENT HISTORY

H/o treatment taken for present illness

H/o. Chemotherapy, radiotherapy

H/o. Steroid therapy / other immunosuppressive drug therapy

H/o. Treatment for HIV

H/o. Treatment for Diabetes, tuberculosis

FAMILY HISTORY

H/o. Varicella in any other family members

PERSONAL HISTORY

H/o. Alcoholism / Smoking

H/o extra marital contact

MENSTRUAL HISTORY

LMP:

RMP**:**

GENERAL EXAMINATION

Built and Nourishment

Pallor, icterus, cyanosis, clubbing, pedal oedema, and lymphadenopathy

VITALS:

PR:

BP:

Temperature:

SYSTEMIC EXAMINATION

CVS:

RS:

Abdomen:

CNS**:**

Sensory

Motor

Cranial nerve

Opthal:

ENT:

DERMATOLOGICAL EXAMINATION

SKIN

•Dermatome involved

• Stages of skin lesions:

Erythema

Papules

Vesicles

Pustules

Crust

• Hyperaesthesia

Complications:

- Secondary infection
- Ulceration
- Post inflammatory hypo/hyperpigmentation
- Scarring
- Post herpetic neuralgia

Clinical diagnosis:

Investigations:

- Tzanck Smear – MNG cells seen Yes / No
- Complete haemogram
- Random blood sugar
- Urine - albumin
  - sugar
  - deposits
- ELISA for HIV
- Biopsy

TREATMENT:

- Topicals
- Antivirals
- Analgesics
- Anticonvulsants
- Antidepressants
- Others
- Specialist opinion

FOLLOW UP VISITS:

CONSENT FORM

Hereby I volunteer and to participate in this study **"ACLINICAL STUDY OF 150 CASES OF HERPES ZOSTER"**Was fully explained about the nature of this study by the doctor, knowing which I **Mr/Mrs…….** fully consent to volunteer in this study.

Date:

Place: **Signature of the volunteer;**

Signature of the doctor:

ஒப்புதல் படிவம்

பெயர் :

வயது :

பாலினம் :

முகவரி :

அரசு கோவை மருத்துவக்கல்லூரியில் மருத்துவபட்ட மேற்படிப்பு பயிலும் மாணவி **ர.வித்யா** அவர்கள் மேற்கொள்ளும் ஆய்வில் முழு சம்மதத்துடனும், சுய சிந்தனையுடனும் கலந்துகொள்ளசம்மதிக்கிறேன். இந்த ஆய்வில் செய்முறைமற்றும் அனைத்துவிளக்கங்களையும் கேட்டுக் கொண்டு எனது சந்தேகங்களை தெளிவுப்படுத்தி கொண்டேன் என்பதை தெரிவித்துக் கொள்கிறேன்.

இடம் :

தேதி :

கையொப்பம் /ரேகை

ஒப்புதல் படிவம்

பெயர் :

வயது :

பாலினம் :

முகவரி :

..... என்ற குழந்தையின் தாய் /தந்தையராகிய நான், அரசு கோவை மருத்துவக்கல்லூரியில் மருத்துவ பட்டமேற்படிப்பு பயிலும் மாணவி **ர.வித்யா** அவர்கள் மேற்கொள்ளும் ஆய்வில் முழு சம்மதத்துடனும், சுய சிந்தனையுடன் அனுமதிக்கிறேன். இந்த ஆய்வில் செய்முறைமற்றும் அனைத்து விளக்கங்களையும் கேட்டுக் கொண்டு எனது சந்தேகங்களை தெளிவுப்படுத்தி கொண்டேன் என்பதை தெரிவித்துக் கொள்கிறேன்.

இடம் :

தேதி :

கையொப்பம் /ரேகை

MASTER CHART

S.No	Name	Age	Sex		PRODROMAL SYMPTOMS								DERMATOMAL INVOLVEMENT					Complications				Investigations	
				First visit toOPD (---Day of illness)	Dermatomal pain	fever	Burning sensation	Itching	paraesthesia	Ear pain	Provacativefactors	past history of chicken pox	cervical	thoracic	lumbar	sacral	trigeminal	P H N	secondary infections	scarring	keloid	Tzanck smear MNG cells	ELISA
1	Venkatesh	38	M	2nd			yes					+	✓										
2	Subramani	55	M	3rd	yes							+		✓									
3	Vellathai	70	F	5th	yes						DM	+				✓		yes	✓			+	
4	sarojini	63	F	3rd	yes							+			✓							+	
5	Aravind	19	M	5th		yes						-		✓								+	
6	Karuppusamy	72	M	2nd	yes							+					✓	Yes					
7	Aruchamy	71	M	5th	yes						DM	+					✓	Yes				+	
8	Sabiya	45	F	4th				yes				+		✓								+	
9	Balkishbanu	28	F	3rd	yes							+	✓									+	
10	Sedhuraman	52	M	5th	yes							+					✓					+	
11	Ramkumar	27	M	2nd								+		✓									
12	Rangammal	80	F	5th	yes							+		✓				yes					
13	Sindhu	24	F	4th		yes						+		✓								+	
14	Rani	58	F	5th	yes							+			✓							+	
15	Vellingiri	55	M	4th	yes						DM	+					✓		✓			+	
16	Mohammed kasim	12	Mch	4th		yes						+		✓								+	
17	Ayyasamy	65	M	3rd	yes						HT	+			✓			yes				+	
18	Karuppayee	62	F	6th	yes							+		✓				yes			✓		
19	Subramanian	80	M	5th	yes					✓		+					✓					+	
20	Periyanayaki	24	F	3rd							HT	+		✓								+	

21	Mohammed rashik11	11	Mch	7th	yes							+		✓								
22	Ramasamy	66	M	3rd	yes							+		✓				yes				
23	Arusamy	57	M	7th	yes						HIV	+	✓	✓				yes				+	+
24	Jakkira	67	F	5th	yes						DM	+	✓					yes				+	
25	Jothinathan	45	M	3rd	yes							-	✓										
26	Ganesh	35	M	6th				yes				+		✓									
27	Meenakshi	96	F	7th	yes							+		✓				yes					
28	Saraswathi	45	F	7th							HT	+				✓							
29	Amalraj	45	M	3rd								+		✓									
30	Muthukumar	34	M	5th	yes							+		✓				yes				+	
31	Muthammal	54	F	4th	yes							+	✓									+	
32	Rahman	10	Mch	3rd		Yes					DM	+				✓						+	
33	Muthusamy	49	M	4th	yes							+		✓				yes				+	
34	Kokila	37	F	3rd								+	✓									+	
35	Kayarnisha	58	F	4th	yes							+		✓				yes	✓			+	
36	Chinnappan	65	M	2nd	yes							+		✓									
37	Mariappan	39	M	4th		yes					HT	+	✓					yes				+	
38	Thangammal	58	F	3rd				yes				+		✓								+	
39	Karthikayeni	57	F	4th	yes							+			✓							+	
40	Gowthaman	18	M	3rd								+	✓									+	
41	Pothiraman	42	M	4th	yes							+		✓				yes				+	
42	Subramani	57	M	4th	yes							-		✓								+	
43	Rathinam	50	F	2nd	yes							+	✓										
44	Shajakhan	32	M	6th		yes						+					✓	yes					
45	Selvam	61	M	4th			yes					+		✓						✓		+	
46	sugitha	59	F	5th	yes							+		✓								+	
47	Rani	50	F	3rd	yes						DM	+			✓							+	
48	Raju	76	M	7th	yes							+		✓						✓			

49	Md.Kajamideen	14	M	4th							HT	+		✓								+	
50	Janaki	80	F	4th	yes							+					✓					+	
51	Pathran	27	M	7th								+	✓										
52	Prabhakaran	50	M	4th	yes						HIV	+		✓				yes				+	+
53	Venkatachalam	54	M	3rd	yes							+		✓								+	
54	Vellathai	70	F	5th	yes							+		✓				yes				+	
55	Subramaniam	55	M	4th	yes							+		✓								+	
56	Ranga	50	F	3rd	yes						Ca	+			✓				✓				
57	Thangaraj	47	M	4th			yes					+		✓								+	
58	Sakthivel	52	M	2nd	yes						DM	+		✓									
59	Selvam	61	M	4th			yes					+		✓								+	
60	Harish	52	M	5th	yes							+		✓				yes				+	
61	Thilakaraj	54	M	3rd								+		✓								+	
62	Kanagaraj	48	M	4th					✓			+					✓					+	
63	Gayathri	2	Fch	6th		Yes						-		✓									
64	Devi	31	F	3rd				yes				-		✓								+	
65	Rajammal	69	F	7th		yes						+		✓				yes					
66	Sivaraman	65	M	4th				Yes				+		✓								+	
67	Mehrannisha	60	F	3rd	yes							+					✓	yes	✓			+	
68	Siva mani	38	F	7th	yes						HT	+		✓									
69	Gomathi	79	F	4th	yes							+					✓					+	
70	Thangaiyan	39	M	7th			yes				DM	+		✓									
71	Veeran	64	M	3rd	yes							+	✓					yes				+	
72	Roja	33	F	10th		yes						+			✓								
73	Vellaiyan	68	M	4th	yes							+		✓								+	
74	Sajakan	32	M	12th								+		✓									
75	Saravanan	28	M	4th			yes				DM	-			✓							+	
76	Rathinammal	75	F	3rd	yes							+					✓						
77	Jeyalakshmi	34	F	14th			yes					+		✓									

78	sundharan	47	M	7th	yes							+	✓									+	
79	Andal	58	F	3rd	yes							+		✓					✓				
80	Raji	30	F	13th			yes					+		✓									
81	Mohammed faizer	56	M	4th	yes							+	✓										
82	Deepa	37	F	2nd								+		✓						✓		+	
83	Bhavani	53	F	4th					✓			+	✓										
84	Ramar	56	M	4th	yes							+		✓					✓			+	
85	Chinnasamy	47	M	5th							DM	+					✓					+	
86	Lakshmanan	55	M	3rd								+		✓								+	
87	Velkumar	46	M	6th	yes							+		✓				yes		✓		+	
88	Sivapeumal	37	M	7th			Yes					+		✓									
89	Senthilvel	45	M	4th								+	✓										
90	Arumugam	56	M	7th	yes							-	✓									+	
91	Jeyakumar	82	M	3rd								+		✓									
92	Ayyammal	64	F	7th	yes							+					✓					+	
93	Stalin	34	M	4th			yes					+		✓									
94	Kavitha	45	F	16th	yes						PT	+		✓				yes				+	
95	Jegan	32	M	16th	yes							+	✓										
96	pradhabh	10	Mch	4th								-				✓							
97	Amudhavan	21	M	3rd				yes			HIV	+		✓									+
98	Rashith	74	M	11th	yes		yes					+	✓									+	
99	Joyanalali	46	M	4th				yes				+					✓			✓		+	
100	Nandhagopal	54	M	7th	yes							+		✓				yes				+	
101	Muthumani	70	F	3rd	yes							-					✓						
102	jothi	23	F	21st		yes						+		✓									
103	Karunagaran	61	M	4th	yes							+					✓	yes					
104	Peter vincent	34	M	3rd								+		✓								+	
105	Balamurugan	38	M	4th	yes							+		✓				yes					
106	Ravi	49	M	4th	yes							+	✓									+	

107	Arockiyam	36	M	2nd							Steroid	+		✓								+	
108	Kannupillai	63	F	7th	yes							+	✓					yes					
109	Vinupriya	28	F	4th								+		✓									
110	Muthusamy	45	M	5th	yes							+	✓									+	
111	Sachin	23	M	3rd				yes				+		✓								+	
112	Saraswathi	71	F	5th					✓			+		✓									
113	Nagaraj	52	M	3rd	yes							+	✓										
114	Banupriya	56	F	7th							HT	+					✓						
115	Bharani	13	M	3rd								+		✓									
116	vijaya	76	F	9th	yes							+	✓										
117	Jeyaseeli	60	F	16th							PT	-		✓									
118	Thangaroja	32	F	4th			Yes					+	✓									+	
119	Narmadha	37	F	17th	yes							+					✓				✓		
120	Radha	40	F	3rd	yes							+		✓								+	
121	Mohanavalli	57	F	4th	yes							+					✓	yes				+	
122	Saravanan	34	M	5th								+		✓								+	
123	Anandhan	43	M	2nd	yes							+		✓									
124	Amirtham	59	F	5th	yes							+	✓									+	
125	Gugapriya	63	F	3rd	yes							+					✓					+	
126	Yogitha	24	F	4th								+		✓								+	
127	Shakila	39	F	3rd	yes							+					✓						
128	Murugesan	47	M	6th	yes							+	✓										
129	Rajavel	54	M	3rd	yes							+					✓					+	
130	Silambarasan	34	M	4th		yes						+	✓									+	
131	Dhenu	59	F	3rd						✓		+		✓				yes					
132	Logambal	57	F	5th	yes							+	✓									+	
133	Jothikumar	49	M	4th	yes							+		✓								+	
134	Geethamani	52	F	4th							DM	+		✓					✓			+	

135	Suren	39	M	2nd	yes		yes			✓		+					✓						
136	Selvi	34	F	7th								+		✓									
137	Nagaraj	53	M	4th				yes				+	✓										+
138	Muthukumar	51	M	4th	yes							+		✓				yes					+
139	Kuppuraj	56	M	3rd	yes							+	✓										
140	Kalaiarasi	43	F	7th	yes							+					✓						
141	Nagarani	65	F	5th	yes							+		✓				yes					+
142	Thangavel	54	M	3rd	yes							-		✓									+
143	Natesan	26	M	4th								+	✓										+
144	kalaiaraj	51	M	4th	yes							+					✓						+
145	Rajesh	23	M	2nd								+	✓										
146	manoj	34	M	4th			yes					+		✓									+
147	Amudha	33	F	5th	yes							+		✓				yes					+
148	Periammal	55	F	3rd						✓		-		✓									
149	Ashok	57	M	4th	yes							+					✓						+
150	Karuppusamy	59	M	4th				yes				+		✓									+